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Patentanmeldung Nr. Patent application No. Demande de brevet n°

99116533.3

Der Präsident des Europäischen Patentamts;
Im Auftrag

For the President of the European Patent Office

Le Président de l'Office européen des brevets
p.o.

I.L.C. HATTEN-HECKMAN

DEN HAAG, DEN
THE HAGUE, 19/10/01
LA HAYE, LE

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Blatt 2 d r Bescheinigung
Sheet 2 of the certificate
Page 2 de l'attestation

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Applicant(s):
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Method for growing stem cells

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51
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Method for growing stem cells

The present invention is related to a method for growing stem cells.

Stem cells are commonly defined as cells which exist for the lifetime of an organism and are able to undergo symmetric and/or asymmetric divisions, to give rise to further stem cells (for preservation of the stem cell pool) and to more differentiated cells with defined life-time (for organ-specific functions). Due to this unique property they are ideal vehicles for somatic gene therapy. They would maintain the transgene for the life-time of the tissue and the organism, and would carry the transgene expression into the differentiated cells. Stem cells may be totipotent (e.g. embryonic stem cells), pluripotent (e.g. hematopoietic stem cells) or unipotent (e.g. keratinocytes, muscle precursor cells).

Although being the aim of many research projects, it has until now being very difficult to grow stem cells, especially lineage-committed stem cells, thereby controlling expansion and differentiation of the stem cells.

The present invention provides a method for growing stem cells comprising the steps of

- providing stem cells with supporters said supporters being genetically modified in order to provide externally regulatable interactions between the supporters and the stem cells;

- applying an external signal for starting or stopping the interactions.

According to the present invention, stem cells are co-incubated with supporters. These supporters are genetically modified to allow a regulatable interaction with the

stem cells. These interactions between the supporters and th stem cells are externally regulatable. "Externally regulatable" defines that the interaction between the supporters and the stem cells is regulated from outside of the supporters.

Preferably, the interactions are based on the secretion or display of substances. These substances, which are secreted or displayed by the supporters control the development of the stem cells. The expansion or differentiation of the stem cells is indirectly controlled by the regulatable interactions of the supporters.

Preferably as external signals may serve the addition or removal of substances, heat, light, sound and/or electromagnetic waves. The only requirement is that these external signals are able to regulate the interactions between the supporters and the stem cells.

Preferably, the supporters are cells. They may be stem cells or non-stem cells. In a preferred embodiment these supporters are forming a micro-environment.

The supporting cells can be further transformed with foreign genes to express a gene product of interest e.g. a protein of the clotting cascade, insulin, enzymes growth factors or the like.

It is believed that the supporters form a micro-environment thus providing cytokines and adhesion molecules as well as direct contact between the stem cells and the supporters. Suitable supporters are skin cells, lung cells, bone marrow stroma cells, or tissue cells.

Suitable secreted or displayed substances are cell based growth factors, protein growth factors, interleukines.

In particular, the supporters are genetically modified with a vector comprising a gene for the substances, e.g. interleukines, protooncogenes, oncogenes, cell cycle control genes, and/or cell based growth factors and a regulatable expression system. A preferred regulatable expression system is the regulatable tetracycline expression system.

Preferred vectors for the transformation of the supporters are the vectors selected from the group consisting of pRetro-tet-off-E6/E7, pRetro-tet-off-U19-tsA58, pUHD15.1-ß-gal-NeoR, pUHD10.3-TGFß3, pUHD10.3-hIL3, pUHD10.3-hIL6, pD12YCVJC-long-CNTF, pD12YCVJC-long-GDNF, pD12YCVJC-short-CNTF and pD12YCVJC-short-GDNF.

Details on these vectors can be found in the examples and the figures.

Cell lines obtainable by genetically modification of cells with the vectors of the present invention form part of the invention.

The present invention further provides a method of curing diseases by gene therapy and/or cell therapy which diseases are related to insufficient, lack or disorder of stem cells, by administering to patients in need thereof, supporters being genetically modified in order to provide externally regulatable interactions between the supporters and the stem cells. Furthermore, any disease related to insufficient expression or activity of a protein or enzyme can be treated by administering supporters and/or stem cells after expansion ex vivo.

Fig. 1 shows the appearance of hIL-3, depending on the addition/removal of doxycycline in vivo.

Fig. 2 shows the shows the appearance of hIL-6 depending on the addition/removal of doxycycline in vivo.

Fig. 3 shows the cloning of growth factor genes.

Fig. 4 to 12 show the sequences of vectors.

The method of the present invention is further explained by the following example:

Example

hIL6 containing transgenic-keratinocytic stem cells support the growth of (sister) keratinocytic stem cells in culture: In these sets of experiments, ELISA assays were performed with supernates obtained from one hIL6 of construct teto-hIL6 containing keratinocytic cell clone derived from a CMV-tTA x teto-SV40 T antigen transgenic mouse, either cultured alone, or with doxycycline included in the culture for 0-12h, 25-50h. This experiment is to test whether the secretion of cytokines affects by doxycycline in culture.

hIL6 promotes the growth of CMV-tTA x teto-SV40Tag transgenic keratino cytic stem cell line drastically by increasing cell numbers. At the presence of hIL6, the growth arrest at G1 compartment is abolished, and cells continue to grow in the presence of doxycycline.

The level of hIL6 in the supernates was slightly inhibited at time point of 12h, and increase again at 50h, up to the level of the control cells, i.e., without doxycycline. Thus, hIL6-containing clone continued to secrete hIL6 despite of the fact that doxycycline was included in the culture.

The data are interpreted as follow: Engineered stem cells support the growth of sister stem cells (internally or externally) in vitro by the combination of the following two mechanisms:

(1) The hIL6 engineered keratinocytic stem cells secrete hIL6 into supernate, target and promote the growth of sister keratinocytic stem cells - an external/heterocrine mechanism.

(2) The gene product of hIL6 engineered keratinocytic stem cells, acts intracytoplasmically, and promotes the growth of itself - an internal/autocrine mechanism.

1. In both events, hIL6 is able to maintain skin in the keratinoytic stem cells compartment, upon the withdraw of doxycycline.

Cytokine-containing keratinocytic stem cells and tracheal epithelial stem cells secrete cytokines known to support the growth of hematopoitic stem cells (HSC):

Using hIL3, hIL6, flk2/flt3Ligand to support the growth of HSC for several weeks in culture, and in comparing to that of stroma cell lines in supporting HSC, has been performed. In the literature there are many published data showing that hIL3, hIL6, flk2/flt3Ligand are essential to support the growth of HSC. These data show that these cytokines are essential in maintaining HSC in culture, and in increasing the transduction efficiency of retroviruses into HSC in the two chamber culture system where the experiments were performed and described in the literature.

Keratinoctic stem cell lines and tracheal epithelial stem cell lines were established from CMV-tTA x tetoCMVm-SV40Tag double transgenic mice (from H. Bujard and S. Efrat).

Stem cells are supported by cytokine-containing transgenic stem cells: in vivo using immunoincompetent mice (nu/nu mice): It is for the purpose of somatic

delivery of growth factors essential for maintenance of human hematopoietic stem cells (HSC) in recipient hosts. The cytokines constructed shown to be functional for HSC are hIL3, hIL6, and flk2/flt3Ligand, and thus are used further for in vivo experiments (below).

Teto-hIL6, teto-hIL3 containing transgenic keratinocytic and tracheal epithelial stem cells derived from CMV-tTA x teto-CMVm-SV40Tag double transgenic mice were pre-cultured on DED (denuded dermis from human cosmetic operation) and implanted subcutaneously (flip-in) into immunoincompetent mice (nude mice).

Blood samples from such nude mice were collected from a tail vein of mice periodically. Sera were separated from blood clots. ELISA tests were performed on serum samples collected. After cytokines were demonstrated to appear in blood, such nude mice ingested doxycycline (1mg/ml) included in the drinking water and blood collected at the time points indicated. As indicated in figures 1 (hIL3) and 2 (hIL-6), hIL3 and hIL6 are shown to appear in the blood reaching a significant amount (14.7 pg/ml for hIL3, 15.9 pg/ml for hIL6), and they were decreased when doxycycline was included the drinking water. Upon removal of doxycycline, hIL3 and hIL6 were shown to increase to higher levels again (41.2 pg/ml for hIL3, and 14.5pg/ml for hIL6). Upon reingestion of doxycycline, the levels of cytokines were shown to decrease to zero.

The mice survive over the 5-6months of experiment without any sign of illness due to the implantation of engineered mouse stem cells delivering human cytokines. The pattern can be cyclic. It is predicted that the protocol will work similarly in the SCID-NOD mice. Thus, in nude mice, we show that the secretion of cytokines such as hIL3 and hIL6 into the blood stream is regulated by doxycycline in the drinking water.

In summary, the above protocol of somatic engineering of immuno-incompetent mice with regulatable delivery of growth factors has been tested and shown to be deliverable to high titers in nu/nu mice. The growth of transgenic keratinocytes and lung epithelial cells, and the delivery of cytokines are shown to be subjected to the regulation of doxycycline (in culture of some cells, such as HETA cells but not other cells, such as a hIL6-containing keratinocytic cell line, when doxycycline is included in the medium); and in vivo when included in the drinking water.

The principle of this protocol can also apply to the support of the growth of stem cells of any kind, such as neural and glial stem cells, in immuno-incompetent mice, as a novel diagnostic tool for evaluating the preclinical and clinical protocols.

Establishment and commercialization of SCID-NOD-hu systems as diagnostics for growth and evaluation of self-renewal property of human neuronal and glial stem cells, clinical protocol and for drug targeting:

The keratinocytic stem cell line and tracheal epithelial stem cell line derived from CMV-tTAxtetoCMVm-SV40Tag double transgenic mice are used in this type of experiment. These cell lines are inserted with cytokine constructs for the somatic delivery of neurotropic factors essential for the survival and maintenance of human adult brain stem cells in recipient hosts. The cytokines constructed are pD12YCV-JC-driven GDNF and CNTF. The transgenic tracheal epithelial stem cells are pre-cultured on DED (dead de-epidermized dermis) and implanted subcutaneously (flip-in) (in the head region) into SCID-NOD mice. The growth of transgenic lung keratinocytic stem cells and epithelial cells, and the delivery of cytokines have been shown to be subjected to the regulation of doxycycline in culture and in vivo when included in the drinking water. The mice survivie over the months of experiment without any sign of illness due to the implantation of engineered mouse cells deliv-

ering human cytokines. The principle of the protocol will work similarly in the SCID-NOD mice for human neurotrophic factors.

Protocol for construction of pD12JCVPLong-CNTF plasmid

Similar strategy and construction protocols held for pD12JCVPLong-GDNF, pD12JCVPshort-CNTF, pD12JCVPshort-GDNF.

1. pD12JCVPLong vector (from E. Beck and J. Henson) was linearized upon NsiI restriction enzyme.

2. The sticky ends of the vector were filled using Klenow fragments of E. coli polymerase I.

3. Digestion of the linearized pD12JCVPLong vector with restriction enzyme XhoI.

4. After digestion, the DNA sample was subjected to gel electrophoresis in 0.8% preparative agarose gel to obtain ca. 6.3 kb DNA fragment (pDl2JCVPLong x NsiI/XhoI).

5. pBS-hCNTF-079 vector (from E. Beck) was linearized with restriction enzyme NotI.

6. The termini of the linearized pBS-hCNTF-079 vector was filled with Klenow fragment of E. coli DNA polymerase I in order to obtain the blunt-end.

7. The linearized and blunt-ended (pBS-hCNTF-079 x NotI) was digested with SahI.

8. After digestion, the DNA sample was subjected to gel electrophoresis in 0.8% preparative agarose gel and the 2469 bp DNA fragment containing CNTF gene was isolated.

9. The blunt- and sticky ended (CNTF x NotI/SahI) fragment (from step 8) was ligated with complementary blunt- and sticky-ended (pD12JCVPLong x NsiI/XhoI) (from step 4) vector.

10. VXL1-blue competent bacteria E. coli was transformed with DNA (from step 9), and ampicillin resistant clones were selected, and characterized to be correct.

Protocol for construction of pRetro-OFF-E6E7 plasmid:

1. pLXSNE6E7 vector (from D. Galloway) was linearized upon EcoRI restriction enzyme digestion.

2. The sticky ends of the vector was filled using Klenow fragments of E.coli DNA polymerase I.

3. The termini of the linearized pLXSNE6E7 was ligated with synthetic adaptor (XhoI-NotI-BglII) purchased from Roth, Karlsruhe.

4. The newly adapted-[pLXSNE6E7 x NotI/BamHI] (step 3) was digested with NotI and BamHI.

5. After digestion, the DNA sample was subjeted to gel electrophoresis in 1% preparative agarose gel to obtain ca. 830 bp fragment of [E6E7 x NotIJBamHI].

6. pRetro-OFF vector was digested with NotI and BamHI.

7. The fragment of [E6E7 x NotI/BamHI] was then inserted into the [pRetro-OFF vector x NotI/BamHI] (step 6).

8. XL1-blue competent bacteria E.coli were transformed with the construct from step 7. Ampicillin resistant clones were selected and characterized to be correct.

Protocol-2 for construction of pRetro-OFF-U19tsA58 plasmid:

1. pZipNEOSV(x) vector (from P. Jat) was digested with BamHI restriction enzyme.

2. After digestion, the DNA sample was electrophoresed in 0.8 % preparative agarose gel to obtain ca 2.6 kb DNA fragment (U19tsA58 x BamHI).

3. pRetro-OFF vector was linearized with restriction enzyme BamHI.

4. The terminal of the linearized pRetro-OFF vector was dephosphoried with Shrimp Alkaline Phophatase (USB) from Amersham.

5. The fragment of (U19tsA58 x BamHI) (from step 2) was then inserted into the (pRetro-OFF vector x BamHI) (from step 4).

6. The XL1-blue competent bacteria E. coli was transformed with DNA (from step 5), and ampicillin resistant clones were selected, and characterized to be correct.

Protocol for the construction of pUHD-transactivator vectors:

A. Transactivator, pUHD15.1-pCMV-tTA-ß-gal-neomycin plasmid:

1. pUHD15.1 (from H. Bujard) was linearized using BamHI restriction enzyme.

2. 5' -end was dephosphorized using phosphatase, and the DNA sample was subjected to gel electrohoresis in 1% preparative agarose gel to obtain ca. 7255 bp fragment of (pUHD15.1BamHI).

3. IRES-ßgeo fragment which contains lacZ+neo (Ca 3050 bp)) was obtained from another plasmid (ptetotsA58IRESßgeo) (from H. Schoeler) using BamHI restriction enzyme digestion.

4. After digestion, the DNA sample was subjected to gel electrohoresis in 1% preparative agarose gel to obtain ca. 3050 bp fragment of (IRES-ßgeoBamHI).

5. The fragement of (IRES-ßgeoBamHI) (step 4) was then inserted into the (pUHD15.1BamHI) (step 2)ß.

6. XL1-blue competent bacteria E. coli were transformed with the construct from step 5. Ampicillin resistant clones were selected and characterized to be correct.

Protocol for the construction of pUHD-responder vectors:

B. Responder pUHD10.3 cytokine plasmids:

1. The multiple cloning site (MCS) of responder pUHD10.3 (from H. Bujard) was linearized using EcoRI and SacII (for hIL6), or EcoRI and BamHI (for hIL3), or EcoRI and XbaI (for TGFß3) restriction enzymes.

2. After digestion, the individual DNA sample was subjected to gel electrohoresis in 1% preparative agarose gel to obtain ca. 3150 bp fragment of DNA.

3. Fragments of cDNA coding for hIL6 (EcoRI-SacII), hIL3 (EcoRI-BamHI), TGFß3 (EcoRI-XbaI) were obtained from the original supplier (A. Bernad, Ge-

netic Institute, ATCC), and individual restriction enzyme digested as indicated in the original publications.

4. After digestion, the DNA sample was subjected to gel electrohoresis in 1% preparative agarose gel to obtain ca. 600 bp fragment of hIL6 (EcoRI-SacII), ca. 475 bp fragment of hIL3 (EcoRI-BamHI). and ca. 1233 bp fragment of TGFß3 (EcoRI-XbaI).

5. The fragement coding for the respective cytokine gene (step 4) was then inserted into the responder pUHD10.3 EcoRI-SacII (for hIL6), or EcoRI-BamHI (for hIL3), or EcoRI-XbaI (for TGFß3) (step 2).

6. XL1-blue competent bacteria E. coli were transformed with the construct from step 5. Ampicillin resistant clones were selected and characterized to be correct.

Claims

1. A method for growing stem cells comprising the steps of

   - providing stem cells with supporters said supporters being genetically modified in order to provide externally regulatable interactions between the supporters and the stem cells;

   - applying an external signal for starting or stopping the interactions.

2. The method of claim 1 wherein the interactions are based on secretion or display of substances.

3. The method of any of the claims 1 or 2 wherein the supporters are modified for the secretion or display of substances under control of a promoter.

4. The method of any of claims 1 to 4 wherein the external signal is the addition or removal of substances, heat, light, sound and/or electromagnetic waves.

5. The method of any of claims 1 to 4, wherein the supporters are non-stem cells.

6. The method of any of claims 1 to 4, wherein the supporters are stem cells.

7. The method of any one of claims 1 to 6, wherein the supporters are forming a micro-environment.

8. The method f any one of claims 1 to 7, wherein the supporters are skin cells, lung cells, bone marrow stroma cells or tissue cells.

9. The method of any one of claims 1 to 8, wherein the supporters are secreting or displaying cell based growth factors, protein growth factors and/or interleukines.

10. The method of any one of claims 1 to 8, wherein the supporters are transformed by a vector comprising a gene for interleukines, protooncogenes, oncogenes, cell cycle control genes, and/or cell based growth factors as well as a regulatable expression system, such as a tetracycline regulatable expression system.

11. A vector selected from the group consisting of pRetro-tet-off-E6/E7, pRetro-tet-off-U19-tsA58, pUHD15.1-ß-gal-NeoR, pUHD10.3-TGFß3, pUHD10.3-hIL3, pUHD10.3-hIL6, pD12YCVJC-long-CNTF, pD12YCVJC-long-GDNF, pD12YCVJC-short-CNTF and pD12YCVJC-short-GDNF.

12. A supporter cell being genetically modified in order to provide a regulatable secretion and/or a display of substances of the supporters.

13. A method of curing diseases by gene therapy and/or cell therapy which diseases are related to insufficient and/or lack and/or disorders of stem cells, by administering to patients in need thereof, supporters being genetically modified in order to provide externally regulatable interaction between supporter cells and stem cells.

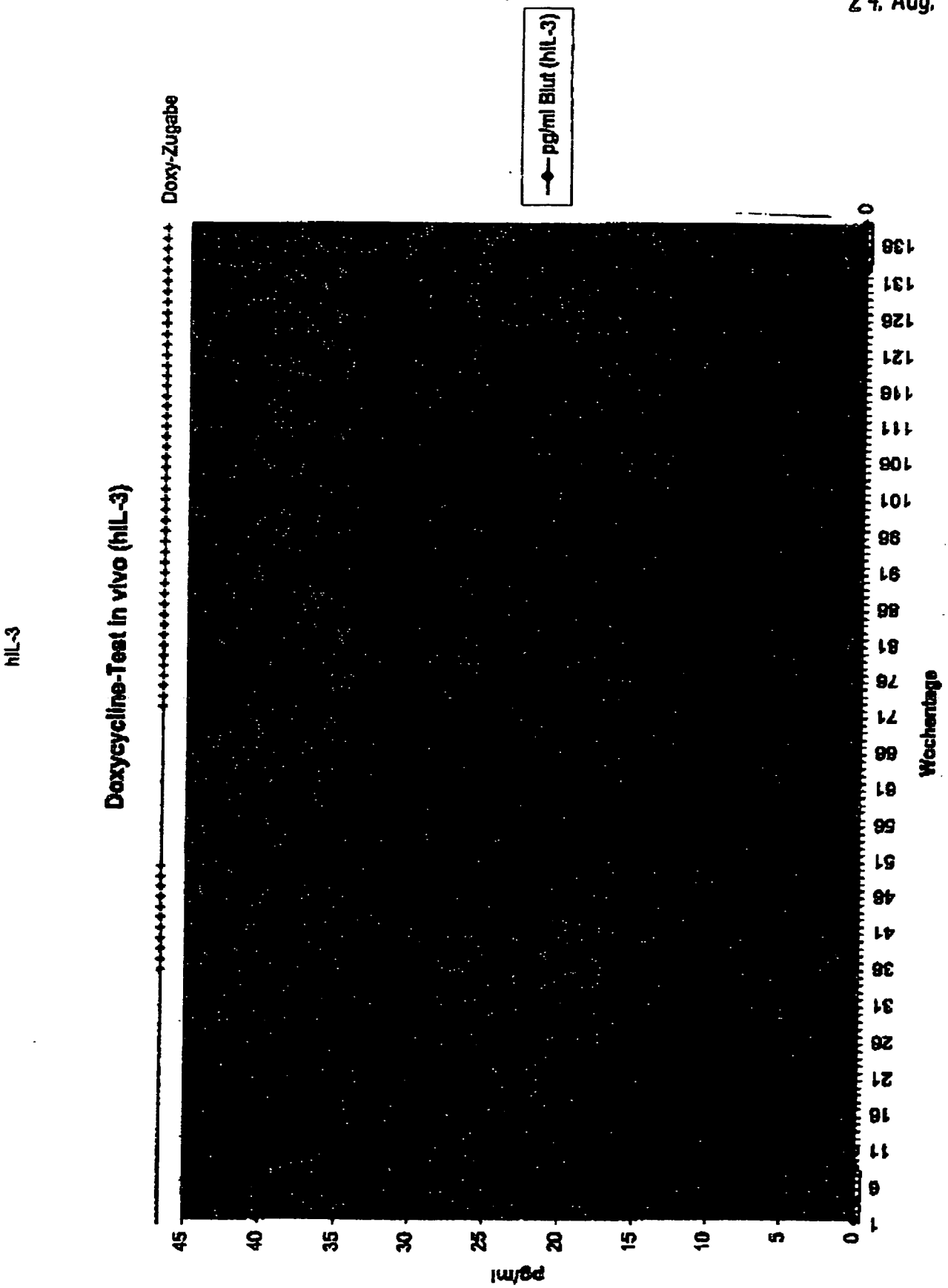
14. Cell lines obtainable by transforming cells with the vector according to claim 11.

Abstract

A method for growing stem cells comprising the steps of

- providing stem cells with supporters said supporters being genetically modified in order to provide externally regulatable interactions between the supporters and the stem cells;

- applying an external signal for starting or stopping the interactions.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hIL-3
Wochentage
pg/ml
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126
121
116
111
106
101
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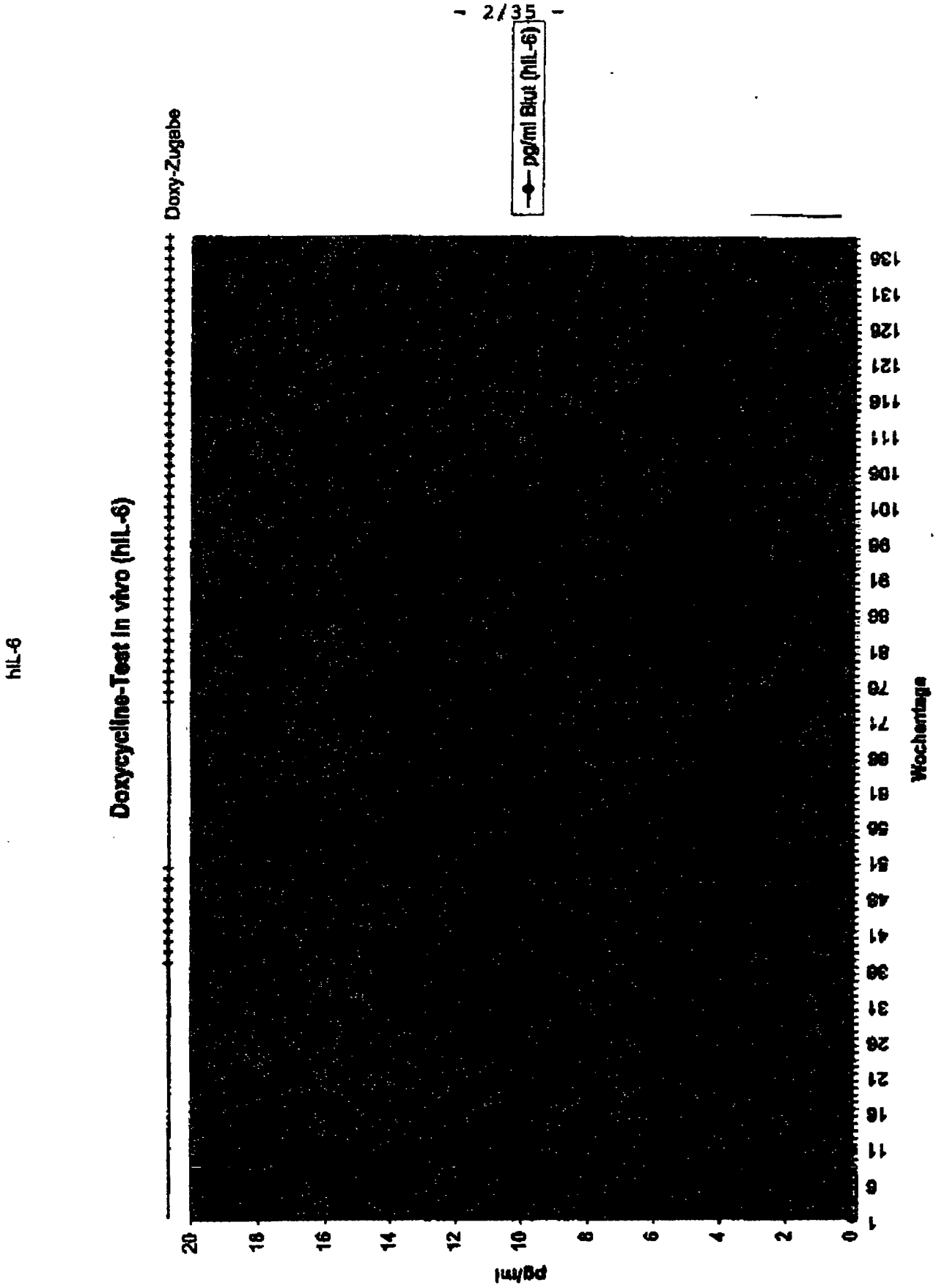
Fig. 1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101
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111
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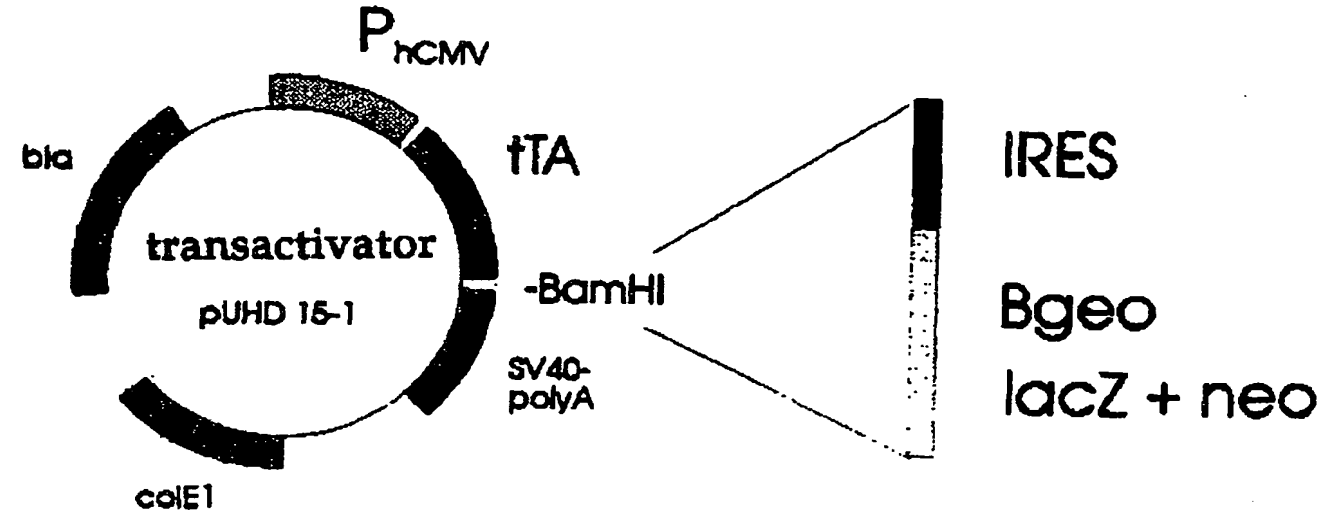
Fig. 2

Cloning of growth factor genes



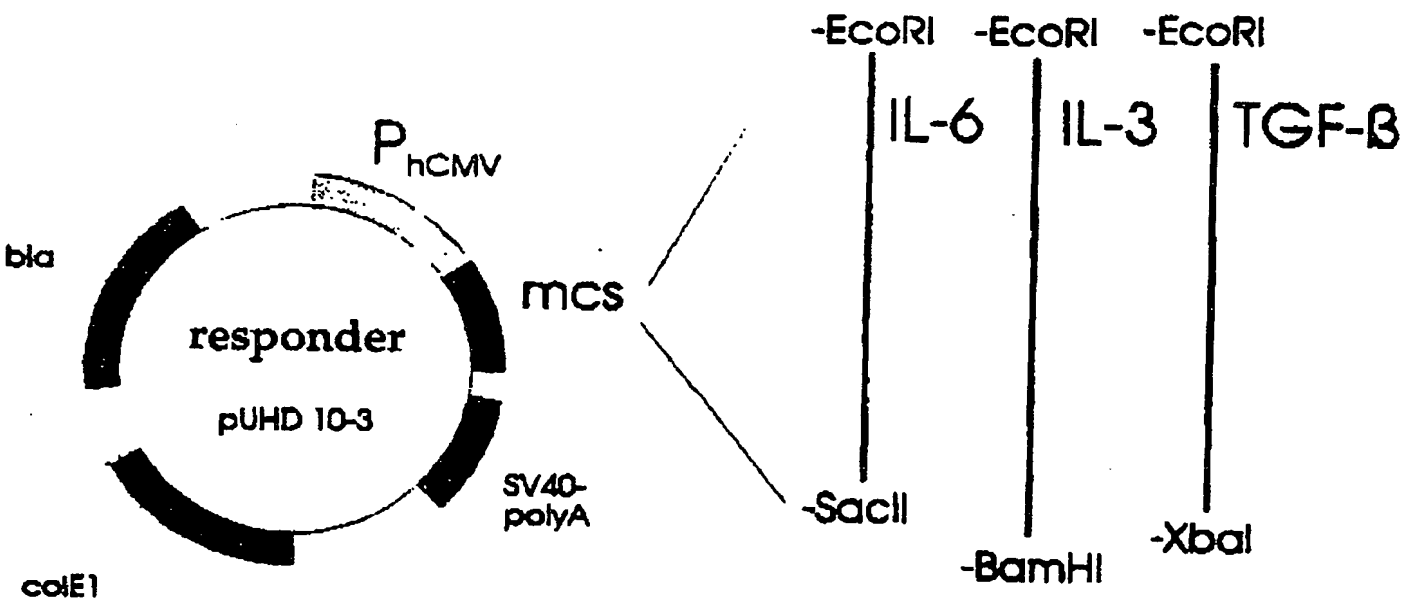


Fig. 3

pD12JCVPlong-hCNTF

Length: 7969 July 22, 1999

```
   1  GCTAGCGATT TAGGTGACAC TATAGAATAG ATCtcg cnn nGTCACCCCT
  51  AGAGTCGAGC TGTGACGGTC CTTACAATGA AATGCANCTG GGTTATCTTC
 101  TTCCTGATGG CAGGGGTTAC AGGTAAGGGG CTCCCAAGTC CCAAACTTGA
 151  GGGTCCATAA ACTCTGTGAC AGTGGCAATC ACTTTGCCTT TCTTTCTACA
 201  GGGGTGAATT CGGCTTTCAC AGAGCATTCA CCGCTGACCC CTCACCGTCG
 251  GGACCTCTGT AGCCGCTCTA TCTGGCTAGC AAGGAAGATT CGTTCAGACC
 301  TTGACTGCTC TTACGGAATC CTATGTAAGT TGCCTATTTT GCTGTTATCT
 351  GTTTTCCCTT CATCTTTTTT GATCCAGCAA CTTACCATCA CGCATCAGCT
 401  CCATTACCAA TTGTGAAAGC TCTAATCATA TAGTCATTCA TATAGGTTAT
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Fig. 4

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2501 ACGATATGGG CTGAATACAA ATCACAGAAT CGTCGTATGC AGTGAAAACT

2551 CTCTTCAATT CTTTATGCCG GTGTTGGGCG CGTTATTTAT CGGAGTTGCA

2601 GTTGCGCCCG CGAACGACAT TTATAATGAA CGTGAATTGC TCAACAGTAT

2651 GAACATTTCG CAGCCTACCG TAGTGTTTGT TTCCAAAAAG GGGTTGCAAA

Fig. 4

2701 AAATTTTGAA CGTGCAAAAA AAATTACCAA TAATCCAGAA AATTATTATC

2751 ATGGATTCTA AAACGGATTA CCAGGGATTT CAGTCGATGT ACACGTTCGT

2801 CACATCTCAT CTACCTCCCG GTTTTAATGA ATACGATTTT GTACCAGAGT

2851 CCTTTGATCG TGACAAAACA ATTGCACTGA TAATGAATTC CTCTGGATCT

2901 ACTGGGTTAC CTAAGGGTGT GGCCCTTCCG CATAGAACTG CCTGCGTCAG

2951 ATTCTCGCAT GCCAGAGATC CTATTTTTGG CAATCAAATC ATTCCGGATA

3001 CTGCGATTTT AAGTGTTGTT CCATTCCATC ACGGTTTTGG AATGTTTACT

3051 ACACTCGGAT ATTTGATATG TGGATTTCGA GTCGTCTTAA TGTATAGATT

3101 TGAAGAAGAG CTGTTTTTAC GATCCCTTCA GGATTACAAA ATTCAAAGTG

3151 CGTTGCTAGT ACCAACCCTA TTTTCATTCT TCGCCAAAAG CACTCTGATT

3201 GACAAATACG ATTTATCTAA TTTACACGAA ATTGCTTCTG GGGGCGCACC

3251 TCTTTCGAAA GAAGTCGGGG AAGCGGTTGC AAAACGCTTC CATCTTCCAG

3301 GGATACGACA AGGATATGGG CTCACTGAGA CTACATCAGC TATTCTGATT

3351 ACACCCGAGG GGGATGATAA ACCGGGCGCG GTCGGTAAAG TTGTTCCATT

3401 TTTTGAAGCG AAGGTTGTGG ATCTGGATAC CGGGAAAACG CTGGGCGTTA

3451 ATCAGAGAGG CGAATTATGT GTCAGAGGAC CTATGATTAT GTCCGGTTAT

3501 GTAAACAATC CGGAAGCGAC CAACGCCTTG ATTGACAAGG ATGGATGGCT

3551 ACATTCTGGA GACATAGCTT ACTGGGACGA AGACGAACAC TTCTTCATAG

3601 TTGACCGCTT GAAGTCTTTA ATTAAATACA AAGGATATCA GGTGGCCCCC

3651 GCTGAATTGG AATCGATATT GTTACAACAC CCCAACATCT TCGACGCGGG

3701 CGTGGCAGGT CTTCCCGACG ATGACGCCGG TGAACTTCCC GCCGCCGTTG

3751 TTGTTTTGGA GCACGGAAAG ACGATGACGG AAAAAGAGAT CGTGGATTAC

3801 GTCGCCAGTC AAGTAACAAC CGCGAAAAAG TTGCGCGGAG GAGTTGTGTT

3851 TGTGGACGAA GTACCGAAAG GTCTTACCGG AAAACTCGAC GCAAGAAAAA

3901 TCAGAGAGAT CCTCATAAAG GCCAAGAAGG GCGGAAAGTC CAAATTGTAA

3951 AATGTAACTG TATTCAGCGA TGACGAAATT CTTAGCTATT GTAATGACTC

4001 TAGAGGATCT TTGTGAAGGA ACCTTACTTC TGTGGTGTGA CATAATTGGA

4051 CAAACTACCT ACAGAGATTT AAAGCTCTAA GGTAAATATA AAATTTTTAA

Fig. 4

```
4101  GTGTATAATG TGTTAAACTA CTGATTCTAA TTGTTTGTGT ATTTTAGATT
4151  CCAACCTATG GAACTGATGA ATGGGAGCAG TGGTGGAATG CCTTTAATGA
4201  GGAAAACCTG TTTTGCTCAG AAGAAATGCC ATCTAGTGAT GATGAGGCTA
4251  CTGCTGACTC TCAACATTCT ACTCCTCCAA AAAAGAAGAG AAAGGTAGAA
4301  GACCCCAAGG ACTTTCCTTC AGAATTGCTA AGTTTTTTGA GTCATGCTGT
4351  GTTTAGTAAT AGAACTCTTG CTTGCTTTGC TATTTACACC ACAAAGGAAA
4401  AAGCTGCACT GCTATACAAG AAAATTATGG AAAAATATTC TGTAACCTTT
4451  ATAAGTAGGC ATAACAGTTA TAATCATAAC ATACTGTTTT TTCTTACTCC
4501  ACACAGGCAT AGAGTGTCTG CTATTAATAA CTATGCTCAA AAATTGTGTA
4551  CCTTTAGCTT TTTAATTTGT AAAGGGGTTA ATAAGGAATA TTTGATGTAT
4601  AGTGCCTTGA CTAGAGATCA TAATCAGCCA TACCACATTT GTAGAGGTTT
4651  TACTTGCTTT AAAAAACCTC CCACACCTCC CCCTGAACCT GAAACATAAA
4701  ATGAATGCAA TTGTTGTTGT TAACTTGTTT ATTGCAGCTT ATAATGGTTA
4751  CAAATAAAGC AATAGCATCA CAAATTTCAC AAATAAAGCA TTTTTTTCAC
4801  TGCATTCTAG TTGTGGTTTG TCCAAACTCA TCAATGTATC TTATCATGTC
4851  TGGATCCCCG GGTCCCTATA GTGAGTCGTA TTAGCTTGGC GTAATCATGG
4901  TCATAGCTGT TTCCTGTGTG AAATTGTTAT CCGCTCACAA TTCCACACAA
4951  CATACGAGCC GGAAGCATAA AGTGTAAAGC CTGGGGTGCC TAATGAGTGA
5001  GCTAACTCAC ATTAATTGCG TTGCGCTCAC TGCCCGCTTT CCAGTCGGGA
5051  AACCTGTCGT GCCAGCTGCA TTAATGAATC GGCCAACGCG CGGGGAGAGG
5101  CGGTTTGCGT ATTGGGCGCT CTTCCGCTTC CTCGCTCACT GACTCGCTGC
5151  GCTCGGTCGT TCGGCTGCGG CGAGCGGTAT CAGCTCACTC AAAGGCGGTA
5201  ATACGGTTAT CCACAGAATC AGGGGATAAC GCAGGAAAGA ACATGTGAGC
5251  AAAAGGCCAG CAAAAGGCCA GGAACCGTAA AAAGGCCGCG TTGCTGGCGT
5301  TTTTCCATAG GCTCCGCCCC CCTGACGAGC ATCACAAAAA TCGACGCTCA
5351  AGTCAGAGGT GGCGAAACCC GACAGGACTA TAAAGATACC AGGCGTTTCC
5401  CCCTGGAAGC TCCCTCGTGC GCTCTCCTGT TCCGACCCTG CCGCTTACCG
5451  GATACCTGTC CGCCTTTCTC CCTTCGGGAA GCGTGGCGCT TTCTCAATGC
```

Fig. 4

```
5501  TCACGCTGTA GGTATCTCAG TTCGGTGTAG GTCGTTCGCT CCAAGCTGGG
5551  CTGTGTGCAC GAACCCCCCG TTCAGCCCGA CCGCTGCGCC TTATCCGGTA
5601  ACTATCGTCT TGAGTCCAAC CCGGTAAGAC ACGACTTATC GCCACTGGCA
5651  GCAGCCACTG GTAACAGGAT TAGCAGAGCG AGGTATGTAG GCGGTGCTAC
5701  AGAGTTCTTG AAGTGGTGGC CTAACTACGG CTACACTAGA AGGACAGTAT
5751  TTGGTATCTG CGCTCTGCTG AAGCCAGTTA CCTTCGGAAA AAGAGTTGGT
5801  AGCTCTTGAT CCGGCAAACA AACCACCGCT GGTAGCGGTG GTTTTTTTGT
5851  TTGCAAGCAG CAGATTACGC GCAGAAAAAA AGGATCTCAA GAAGATCCTT
5901  TGATCTTTTC TACGGGGTCT GACGCTCAGT GGAACGAAAA CTCACGTTAA
5951  GGGATTTTGG TCATGAGATT ATCAAAAAGG ATCTTCACCT AGATCCTTTT
6001  AAATTAAAAA TGAAGTTTTA AATCAATCTA AAGTATATAT GAGTAAACTT
6051  GGTCTGACAG TTACCAATGC TTAATCAGTG AGGCACCTAT CTCAGCGATC
6101  TGTCTATTTC GTTCATCCAT AGTTGCCTGA CTCCCCGTCG TGTAGATAAC
6151  TACGATACGG GAGGGCTTAC CATCTGGCCC CAGTGCTGCA ATGATACCGC
6201  GAGACCCACG CTCACCGGCT CCAGATTTAT CAGCAATAAA CCAGCCAGCC
6251  GGAAGGGCCG AGCGCAGAAG TGGTCCTGCA ACTTTATCCG CCTCCATCCA
6301  GTCTATTAAT TGTTGCCGGG AAGCTAGAGT AAGTAGTTCG CCAGTTAATA
6351  GTTTGCGCAA CGTTGTTGCC ATTGCTACAG GCATCGTGGT GTCACGCTCG
6401  TCGTTTGGTA TGGCTTCATT CAGCTCCGGT TCCCAACGAT CAAGGCGAGT
6451  TACATGATCC CCCATGTTGT GCAAAAAAGC GGTTAGCTCC TTCGGTCCTC
6501  CGATCGTTGT CAGAAGTAAG TTGGCCGCAG TGTTATCACT CATGGTTATG
6551  GCAGCACTGC ATAATTCTCT TACTGTCATG CCATCCGTAA GATGCTTTTC
6601  TGTGACTGGT GAGTACTCAA CCAAGTCATT CTGAGAATAG TGTATGCGGC
6651  GACCGAGTTG CTCTTGCCCG GCGTCAATAC GGGATAATAC CGCGCCACAT
6701  AGCAGAACTT TAAAAGTGCT CATCATTGGA AAACGTTCTT CGGGGCGAAA
6751  ACTCTCAAGG ATCTTACCGC TGTTGAGATC CAGTTCGATG TAACCCACTC
6801  GTGCACCCAA CTGATCTTCA GCATCTTTTA CTTTCACCAG CGTTTCTGGG
6851  TGAGCAAAAA CAGGAAGGCA AAATGCCGCA AAAAAGGGAA TAAGGGCGAC
```

Fig. 4

```
6901  ACGGAAAATGT TGAATACTCA TACTCTTCCT TTTTCAATAT TATTGAAGCA

6951  TTTATCAGGG TTATTGTCTC ATGAGCGGAT ACATATTTGA ATGTATTTAG

7001  AAAAATAAAC AAATAGGGGT TCCGCGCACA TTTCCCCGAA AAGTGCCACC

7051  TGACGTCTAA GAAACCATTA TTATCATGAC ATTAACCTAT AAAAATAGGC

7101  GTATCACGAG GCCCTTTCGT CTCGCGCGTT TCGGTGATGA CGGTGAAAAC

7151  CTCTGACACA TGCAGCTCCC GGAGACGGTC ACAGCTTGTC TGTAAGCGGA

7201  TGCCGGGAGC AGACAAGCCC GTCAGGGCGC GTCAGCGGGT GTTGGCGGGT

7251  GTCGGGGCTG GCTTAACTAT GCGGCATCAG AGCAGATTGT ACTGAGAGTG

7301  CACCATATGC GGTGTGAAAT ACCGCACAGA TGCGTAAGGA GAAAATACCG

7351  CATCAGGCGC CATTCGCCAT TCAGGCTGCG CAACTGTTGG GAAGGGCGAT

7401  CGGTGCGGGC CTCTTCGCTA TTACGCCAGC TGGCGAAAGG GGGATGTGCT

7451  GCAAGGCGAT TAAGTTGGGT AACGCCAGGG TTTTCCCAGT CACGACGTTG

7501  TAAAACGACG GCCAGTGAAT TTCGACCTGC AGTCGACAGA AGCCTTACGT

7551  GACAGCTGGC GAAGAACCAT GGCCAGCTGG TGACAAGCCA AAACAGCTCT

7601  GGCTCGCAAA ACATGTTCCC TTGGCTGCTT TCCACTTCCC CTTGTGCTTT

7651  GTTTACTTGT GTCAGCTGGT TGGCTCCCTA GGTATGAGCT CATGCTTGGC

7701  TGGCAGCCAT CCAGTTTTAG CCAGCTCTGC TTTGTTTACT TGTGTCAGCT

7751  GGTTGGCTCC CTAGGTATGA GCTCATGCTT GGCTGGCAGC CATCCAGTTT

7801  TAGCCAGCTC CTCCCTACCT TCCCTTTTTT TTATATATAC AGGAGGCCGA

7851  GGCCGCCTCC GCCTCCAAGC TTACTCAGAA GTAGTAAGGG CGTGGAGGCT

7901  TTTTAGGAGG CCAGGGAAAT TCCCTTGTTT TTCCCTTTTT TGCAGTAATT

7951  TTTTGCTGCA AAAAGCTAA
```

Fig. 4

JCVPlong-gdnf Length: 6971 June 8, 1999 16:42 Type: N Check: 3588 ..

```
   1  GCTAGCGATT TAGGTGACAC TATAGAATAG ATCCCCATGA AGTTATGGGA
  51  TGTCGTGGCT GTCTGCCTGG TGCTGCTCCA CACCGCGTCC GCCTTCCCGC
 101  TGCCCGCCGG TAAGAGGCCT CCCGAGGCGC CCGCCGAAGA CCGCTCCCTC
 151  GGCCGCCGCC GCGCGCCCTT CGCGCTGAGC AGTGACTCAA ATATGCCAGA
 201  GGATTATCCT GATCAGTTCG ATGATGTCAT GGATTTTATT CAAGCCACCA
 251  TTAAAAGACT GAAAAGGTCA CCAGATAAAC AAATGGCAGT GCTTCCTAGA
 301  AGAGAGCGGA ATCGCCAGGC TGCAGCTGCC AACCCAGAGA ATTCCAGAGG
 351  AAAAGGTCGG AGAGGCCAGA GGGGCAAAAA CCGGGGTTGT GTCTTAACTG
 401  CAATACATTT AAATGTCACT GACTTGGGTC TGGGCTATGA AACCAAGGAG
 451  GAACTGATTT TTAGGTACTG CAGCGGCTCT TGCGATGCAG CTGAGACAAC
 501  GTACGACAAA ATATTGAAAA ACTTATCCAG AAATAGAAGG CTGGTGAGTG
 551  ACAAAGTAGG GCAGGCATGT TGCAGACCCA TCGCCTTTGA TGATGACCTG
 601  TCGTTTTTAG ATGATAACCT GGTTTACCAT ATTCTAAGAA AGCATTCCGC
 651  TAAAAGGTGT GGATGTATCT GACTGGTGCG CCGTCTTTCC CGACGTTAAA
 701  GGGATGAAAC CACAAGACTT ACCTTCGCTC GGAAGTAAAA CGACAAACAC
 751  ACACAGTTTT GCCCGTTTTC ATGAGAAATG GGACGTCTGC GCACGAAACG
 801  CGCCGTCGCT TGAGGAGGAC TTGTACAAAC ACGATCTATG CAGGTTTCCC
 851  CAACTGACAC AAACCGTGCA ACTTGAAACT CCGCCTGGTC TTTCCAGGTC
 901  TAGAGGGGTA ACATTTTGTA CTGTGTTTGA CTCCACGCTC GATCCACTAG
 951  CGAGTGTTAG TAGCGGTACT GCTGTCTCGT AGCGGAGCAT GTTGGCCGTG
1001  GGAACACCTC CTTGGTAACA AGGACCCACG GGGCCGAAAG CCATGTCCTA
1051  ACGGACCCAA CATGTGTGCA ACCCCAGCAC GGCAGCTTTA CTGTGAAACC
1101  CACTTCAAGC TGACATTGAT ACTGGTACTC AAACACTGGT GACAGGCTAA
1151  GGATGCCCTT CAGGTACCCC GAGGTAACAA GCGACACTCG GGATCTGAGA
1201  AGGGGACTGG GACTTCTTTA AAGTGCCCAG TTTAAAAAGC TTCTACGCCT
1251  GAATAGGTGA CCGGAGGCCG GCACCTTTCC TTTTATAACC ACTGAACACA
1301  TGGAAGACGC CAAAAACATA AAGAAAGGCC CGGCGCCATT CTATCCTCTA
1351  GAGGATGGAA CCGCTGGAGA GCAACTGCAT AAGGCTATGA AGAGATACGC
1401  CCTGGTTCCT GGAACAATTG CTTTTACAGA TGCACATATC GAGGTGAACA
1451  TCACGTACGC GGAATACTTC GAAATGTCCG TTCGGTTGGC AGAAGCTATG
1501  AAACGATATG GGCTGAATAC AAATCACAGA ATCGTCGTAT GCAGTGAAAA
1551  CTCTCTTCAA TTCTTTATGC CGGTGTTGGG CGCGTTATTT ATCGGAGTTG
1601  CAGTTGCGCC CGCGAACGAC ATTTATAATG AACGTGAATT GCTCAACAGT
1651  ATGAACATTT CGCAGCCTAC CGTAGTGTTT GTTTCCAAAA AGGGGTTGCA
1701  AAAAATTTTG AACGTGCAAA AAAAATTACC AATAATCCAG AAAATTATTA
1751  TCATGGATTC TAAAACGGAT TACCAGGGAT TTCAGTCGAT GTACACGTTC
1801  GTCACATCTC ATCTACCTCC CGGTTTTAAT GAATACGATT TTGTACCAGA
1851  GTCCTTTGAT CGTGACAAAA CAATTGCACT GATAATGAAT TCCTCTGGAT
1901  CTACTGGGTT ACCTAAGGGT GTGGCCCTTC CGCATAGAAC TGCCTGCGTC
1951  AGATTCTCGC ATGCCAGAGA TCCTATTTTT GGCAATCAAA TCATTCCGGA
2001  TACTGCGATT TTAAGTGTTG TTCCATTCCA TCACGGTTTT GGAATGTTTA
2051  CTACACTCGG ATATTTGATA TGTCGATTTC GAGTCGTCTT AATGTATAGA
2101  TTTGAAGAAG AGCTGTTTTT ACGATCCCTT CAGGATTACA AAATTCAAAG
2151  TGCGTTGCTA GTACCAACCC TATTTTCATT CTTCGCCAAA AGCACTCTGA
2201  TTGACAAATA CGATTTATCT AATTTACACG AAATTGCTTC TGGGGGCGCA
2251  CCTCTTTCGA AAGAAGTCGG GGAAGCGGTT GCAAAACGCT TCCATCTTCC
2301  AGGGATACGA CAAGGATATG GGCTCACTGA GACTACATCA GCTATTCTGA
2351  TTACACCCGA GGGGGATGAT AAACCGGGCG CGGTCGGTAA AGTTGTTCCA
2401  TTTTTTGAAG CGAAGGTTGT GGATCTGGAT ACCGGGAAAA CGCTGGGCGT
2451  TAATCAGAGA GGCGAATTAT GTGTCAGAGG ACCTATGATT ATGTCCGGTT
2501  ATGTAAACAA TCCGGAAGCG ACCAACGCCT TGATTGACAA GGATGGATGG
2551  CTACATTCTG GAGACATAGC TTACTGGGAC GAAGACGAAC ACTTCTTCAT
2601  AGTTGACCGC TTGAAGTCTT TAATTAAATA CAAAGGATAT CAGGTGGCCC
2651  CCGCTGAATT GGAATCGATA TTGTTACAAC ACCCCAACAT CTTCGACGCG
2701  GGCGTGGCAG GTCTTCCCGA CGATGACGCC GGTGAACTTC CCGCCGCCGT
2751  TGTTGTTTTG GAGCACGGAA AGACGATGAC GGAAAAAGAG ATCGTGGATT
2801  ACGTCGCCAG TCAAGTAACA ACCGCGAAAA AGTTGCGCGG AGGAGTTGTG
2851  TTTGTGGACG AAGTACCGAA AGGTCTTACC GGAAAACTCG ACGCAAGAAA
2901  AATCAGAGAG ATCCTCATAA AGGCCAAGAA GGGCGGAAAG TCCAAATTGT
2951  AAAATGTAAC TGTATTCAGC GATGACGAAA TTCTTAGCTA TTGTAATGAC
3001  TCTAGAGGAT CTTTGTGAAG GAACCTTACT TCTGTGGTGT GACATAATTG
3051  GACAAACTAC CTACAGAGAT TTAAAGCTCT AAGGTAAATA TAAAATTTTT
3101  AAGTGTATAA TGTGTTAAAC TACTGATTCT AATTGTTTGT GTATTTTAGA
3151  TTCCAACCTA TGGAACTGAT GAATGGGAGC AGTGGTGGAA TGCCTTTAAT
3201  GAGGAAAACC TGTTTTGCTC AGAAGAAATG CCATCTAGTG ATGATGAGGC
```

Fig. 5

```
3251  TACTGCTGAC TCTCAACATT CTACTCCTCC AAAAAAGAAG AGAAAGGTAG
3301  AAGACCCCAA GGACTTTCCT TCAGAATTGC TAAGTTTTTT GAGTCATGCT
3351  GTGTTTAGTA ATAGAACTCT TGCTTGCTTT GCTATTTACA CCACAAAGGA
3401  AAAAGCTGCA CTGCTATACA AGAAAATTAT GGAAAAATAT TCTGTAACCT
3451  TTATAAGTAG GCATAACAGT TATAATCATA ACATACTGTT TTTTCTTACT
3501  CCACACAGGC ATAGAGTGTC TGCTATTAAT AACTATGCTC AAAAATTGTG
3551  TACCTTTAGC TTTTTAATTT GTAAAGGGGT TAATAAGGAA TATTTGATGT
3601  ATAGTGCCTT GACTAGAGAT CATAATCAGC CATACCACAT TTGTAGAGGT
3651  TTTACTTGCT TTAAAAAACC TCCCACACCT CCCCCTGAAC CTGAAACATA
3701  AAATGAATGC AATTGTTGTT GTTAACTTGT TTATTGCAGC TTATAATGGT
3751  TACAAATAAA GCAATAGCAT CACAAATTTC ACAAATAAAG CATTTTTTTC
3801  ACTGCATTCT AGTTGTGGTT TGTCCAAACT CATCAATGTA TCTTATCATG
3851  TCTGGATCCC CGGGTCCCTA TAGTGAGTCG TATTAGCTTG GCGTAATCAT
3901  GGTCATAGCT GTTTCCTGTG TGAAATTGTT ATCCGCTCAC AATTCCACAC
3951  AACATACGAG CCGGAAGCAT AAAGTGTAAA GCCTGGGGTG CCTAATGAGT
4001  GAGCTAACTC ACATTAATTG CGTTGCGCTC ACTGCCCGCT TTCCAGTCGG
4051  GAAACCTGTC GTGCCAGCTG CATTAATGAA TCGGCCAACG CGCGGGGAGA
4101  GGCGGTTTGC GTATTGGGCG CTCTTCCGCT TCCTCGCTCA CTGACTCGCT
4151  GCGCTCGGTC GTTCGGCTGC GGCGAGCGGT ATCAGCTCAC TCAAAGGCGG
4201  TAATACGGTT ATCCACAGAA TCAGGGGATA ACGCAGGAAA GAACATGTGA
4251  GCAAAAGGCC AGCAAAAGGC CAGGAACCGT AAAAAGGCCG CGTTGCTGGC
4301  GTTTTTCCAT AGGCTCCGCC CCCCTGACGA GCATCACAAA AATCGACGCT
4351  CAAGTCAGAG GTGGCGAAAC CCGACAGGAC TATAAAGATA CCAGGCGTTT
4401  CCCCCTGGAA GCTCCCTCGT GCGCTCTCCT GTTCCGACCC TGCCGCTTAC
4451  CGGATACCTG TCCGCCTTTC TCCCTTCGGG AAGCGTGGCG CTTTCTCAAT
4501  GCTCACGCTG TAGGTATCTC AGTTCGGTGT AGGTCGTTCG CTCCAAGCTG
4551  GGCTGTGTGC ACGAACCCCC CGTTCAGCCC GACCGCTGCG CCTTATCCGG
4601  TAACTATCGT CTTGAGTCCA ACCCGGTAAG ACACGACTTA TCGCCACTGG
4651  CAGCAGCCAC TGGTAACAGG ATTAGCAGAG CGAGGTATGT AGGCGGTGCT
4701  ACAGAGTTCT TGAAGTGGTG GCCTAACTAC GGCTACACTA GAAGGACAGT
4751  ATTTGGTATC TGCGCTCTGC TGAAGCCAGT TACCTTCGGA AAAAGAGTTG
4801  GTAGCTCTTG ATCCGGCAAA CAAACCACCG CTGGTAGCGG TGGTTTTTTT
4851  GTTTGCAAGC AGCAGATTAC GCGCAGAAAA AAAGGATCTC AAGAAGATCC
4901  TTTGATCTTT TCTACGGGGT CTGACGCTCA GTGGAACGAA AACTCACGTT
4951  AAGGGATTTT GGTCATGAGA TTATCAAAAA GGATCTTCAC CTAGATCCTT
5001  TTAAATTAAA AATGAAGTTT TAAATCAATC TAAAGTATAT ATGAGTAAAC
5051  TTGGTCTGAC AGTTACCAAT GCTTAATCAG TGAGGCACCT ATCTCAGCGA
5101  TCTGTCTATT TCGTTCATCC ATAGTTGCCT GACTCCCCGT CGTGTAGATA
5151  ACTACGATAC GGGAGGGCTT ACCATCTGGC CCCAGTGCTG CAATGATACC
5201  GCGAGACCCA CGCTCACCGG CTCCAGATTT ATCAGCAATA AACCAGCCAG
5251  CCGGAAGGGC CGAGCGCAGA AGTGGTCCTG CAACTTTATC CGCCTCCATC
5301  CAGTCTATTA ATTGTTGCCG GGAAGCTAGA GTAAGTAGTT CGCCAGTTAA
5351  TAGTTTGCGC AACGTTGTTG CCATTGCTAC AGGCATCGTG GTGTCACGCT
5401  CGTCGTTTGG TATGGCTTCA TTCAGCTCCG GTTCCCAACG ATCAAGGCGA
5451  GTTACATGAT CCCCCATGTT GTGCAAAAAA GCGGTTAGCT CCTTCGGTCC
5501  TCCGATCGTT GTCAGAAGTA AGTTGGCCGC AGTGTTATCA CTCATGGTTA
5551  TGGCAGCACT GCATAATTCT CTTACTGTCA TGCCATCCGT AAGATGCTTT
5601  TCTGTGACTG GTGAGTACTC AACCAAGTCA TTCTGAGAAT AGTGTATGCG
5651  GCGACCGAGT TGCTCTTGCC CGGCGTCAAT ACGGGATAAT ACCGCGCCAC
5701  ATAGCAGAAC TTTAAAAGTG CTCATCATTG GAAAACGTTC TTCGGGGCGA
5751  AAACTCTCAA GGATCTTACC GCTGTTGAGA TCCAGTTCGA TGTAACCCAC
5801  TCGTGCACCC AACTGATCTT CAGCATCTTT TACTTTCACC AGCGTTTCTG
5851  GGTGAGCAAA AACAGGAAGG CAAAATGCCG CAAAAAAGGG AATAAGGGCG
5901  ACACGGAAAT GTTGAATACT CATACTCTTC CTTTTTCAAT ATTATTGAAG
5951  CATTTATCAG GGTTATTGTC TCATGAGCGG ATACATATTT GAATGTATTT
6001  AGAAAAATAA ACAAATAGGG GTTCCGCGCA CATTTCCCCG AAAAGTGCCA
6051  CCTGACGTCT AAGAAACCAT TATTATCATG ACATTAACCT ATAAAAATAG
6101  GCGTATCACG AGGCCCTTTC GTCTCGCGCG TTTCGGTGAT GACGGTGAAA
6151  ACCTCTGACA CATGCAGCTC CCGGAGACGG TCACAGCTTG TCTGTAAGCG
6201  GATGCCGGGA GCAGACAAGC CCGTCAGGGC GCGTCAGCGG GTGTTGGCGG
6251  GTGTCGGGGC TGGCTTAACT ATGCGGCATC AGAGCAGATT GTACTGAGAG
6301  TGCACCATAT GCGGTGTGAA ATACCGCACA GATGCGTAAG GAGAAAATAC
6351  CGCATCAGGC CCCATTCGCC ATTCAGGCTG CGCAACTGTT GGGAAGGGCG
6401  ATCGGTGCGG GCCTCTTCGC TATTACGCCA GCTGGCGAAA GGGGGATGTG
6451  CTGCAAGGCG ATTAAGTTGG GTAACGCCAG GGTTTTCCCA GTCACGACGT
6501  TGTAAAACGA CGGCCAGTGA ATTTCGACCT GCAGTCGACA GAAGCCTTAC
6551  GTGACAGCTG GCGAAGAACC ATGGCCAGCT GGTGACAAGC CAAAACAGCT
```

Fig. 5

```
6601  CTGGCTCGCA AAACATGTTC CCTTGGCTGC TTTCCACTTC CCCTTGTGCT
6651  TTGTTTACTT GTGTCAGCTG GTTGGCTCCC TAGGTATGAG CTCATGCTTG
6701  GCTGGCAGCC ATCCAGTTTT AGCCAGCTCT GCTTTGTTTA CTTGTGTCAG
6751  CTGGTTGGCT CCCTAGGTAT GAGCTCATGC TTGGCTGGCA GCCATCCAGT
6801  TTTAGCCAGC TCCTCCCTAC CTTCCCTTTT TTTTATATAT ACAGGAGGCC
6851  GAGGCCGCCT CCGCCTCCAA GCTTACTCAG AAGTAGTAAG GGCGTGGAGG
6901  CTTTTTAGGA GGCCAGGGAA ATTCCCTTGT TTTTCCCTTT TTTGCAGTAA
6951  TTTTTTGCTG CAAAAAGCTA A
```

Fig. 5

pD12JCVPshort-hCNTF

Length: 7558

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   1  GCTAGCGATT TAGGTGACAC TATAGAATCt cgacnnGTCA CCCCTAGAGT
  51  CGAGCTGTGA CGGTCCTTAC AATGAAATGC ANCTGGGTTA TCTTCTTCCT
 101  GATGGCAGGG GTTACAGGTA AGGGGCTCCC AAGTCCCAAA CTTGAGGGTC
 151  CATAAACTCT GTGACAGTGG CAATCACTTT GCCTTTCTTT CTACAGGGGT
 201  GAATTCGGCT TTCACAGAGC ATTCACCGCT GACCCCTCAC CGTCGGGACC
 251  TCTGTAGCCG CTCTATCTGG CTAGCAAGGA AGATTCGTTC AGACCTTGAC
 301  TGCTCTTACG GAATCCTATG TAAGTTGCCT ATTTTGCTGT TATCTGTTTT
 351  CCCTTCATCT TTTTTGATCC AGCAACTTAC CATCACGCAT CAGCTCCATT
 401  ACCAATTGTG AAAGCTCTAA TCATATAGTC ATTCATATAG GTTATTTGAC
 451  ATGGGCCCTT CCCTTGAGGA AACCCATGTG ACTTTATTTT CTTCCTCTGG
 501  GCTGTTTAGG AGATGAAGTT ACTTGAATGA GAAAATATAT ATGGAGTTCT
 551  AGAAAGGATT GGTTTATATG TCTTGGAGGC TATTTCAAAA TTTATTTGGC
 601  CATATATTCT GAATACTACC TAGAACAGAT TAGCCATGGG CCCTNTGGGT
 651  TNTTCATAAG CCATTGTTCT GAANTTTTTT AGCTTTGTAA ATGAAAGGTT
 701  TATGGGATAG GAAGAGTNCT ATGAACGTGG GAGGAATTTG TAAATCCTAC
 751  CAATTTNTNC TATATAGCAT TAGCCCCCAC CTTTTANTAT TCTGCATCAA
 801  AAGTAAGATT GTGTCTAAAG AGAAAGGTNA GCTATCAAAA GGACTCCTAT
 851  AANATTCNTT GGAAACTTNT GGAANTGTCA AATTTNTTTG AGCTAATTNT
 901  TGGAGTTCCA AANTTTGTCT TNTNACAGTN AAGGGGGANC CCCATTCANA
 951  TTTNCCCCCC TNNNGANAAT GCTTGGGGGA AAAAACCTNC CAACCCCNTT
1001  GTGGGANGAA GTTTTTTTAA NNTTTTAAGG CTNGNNGAAA CNGGNTTTTA
1051  ATTTTTTGGG NCNANCGCCT NTCCCCGGTA CCAGGAAAAT CAGGACCTNT
1101  TTTTGGGGNN GNGCNCCNAC NGGGGGGNAA AANGGGAAAT TTCNTCANAA
1151  AAAATCTTTT CCGnnnnnng tgaagcatca gggcctgaac aagaacatca
1201  acctggactc tgcggatggg atgccagtgg caagcactga tcagtggagt
1251  gagctg ccg aggcagagcg actccaagag aaccttcaag cttatcgtac
```

Fig. 6

1301 cttccatgtt ttgttggcca ggctcttaga aga cagcag gtgcatttta

1351 ccccaa cga aggtgacttc catcaagcta tacataccct tcttctccaa

1401 gtcgctgcct ttgcat cca gatagaggag ttaatgat c tcctggaata

1451 caag tcccc cgcaatgagg ctgatgggat gcctattaat gttgg gatg

1501 gtggtctctt tgagaagaag ctgtggggcc taaaggtgct gcaggagctt

1551 tcacagtgga cagtaaggtc catccatgac cttcgtttca tttcttctca

1601 tcagactggg atcccagcac gtgggagcca ttatattgct aacaacaaga

1651 aaatgtagmn nnngcggcct GCGCCGTCTT TCCCGACGTT AAAGGGATGA

1701 AACCACAAGA CTTACCTTCG CTCGGAAGTA AAACGACAAA CACACACAGT

1751 TTTGCCCGTT TTCATGAGAA ATGGGACGTC TGCGCACGAA ACGCGCCGTC

1801 GCTTGAGGAG GACTTGTACA AACACGATCT ATGCAGGTTT CCCCAACTGA

1851 CACAAACCGT GCAACTTGAA ACTCCGCCTG GTCTTTCCAG GTCTAGAGGG

1901 GTAACATTTT GTACTGTGTT TGACTCCACG CTCGATCCAC TAGCGAGTGT

1951 TAGTAGCGGT ACTGCTGTCT CGTAGCGGAG CATGTTGGCC GTGGGAACAC

2001 CTCCTTGGTA ACAAGGACCC ACGGGGCCGA AAGCCATGTC CTAACGGACC

2051 CAACATGTGT GCAACCCCAG CACGGCAGCT TTACTGTGAA ACCCACTTCA

2101 AGGTGACATT GATACTGGTA CTCAAACACT GGTGACAGGC TAAGGATGCC

2151 CTTCAGGTAC CCCGAGGTAA CAAGCGACAC TCGGGATCTG AGAAGGGGAC

2201 TGGGACTTCT TTAAAGTGCC CAGTTTAAAA AGCTTCTACG CCTGAATAGG

2251 TGACCGGAGG CCGGCACCTT TCCTTTTATA ACCACTGAAC ACATGGAAGA

2301 CGCCAAAAAC ATAAAGAAAG GCCCGGCGCC ATTCTATCCT CTAGAGGATG

2351 GAACCGCTGG AGAGCAACTG CATAAGGCTA TGAAGAGATA CGCCCTGGTT

2401 CCTGGAACAA TTGCTTTTAC AGATGCACAT ATCGAGGTGA ACATCACGTA

2451 CGCGGAATAC TTCGAAATGT CCGTTCGGTT GGCAGAAGCT ATGAAACGAT

2501 ATGGGCTGAA TACAAATCAC AGAATCGTCG TATGCAGTGA AAACTCTCTT

2551 CAATTCTTTA TGCCGGTGTT GGGCGCGTTA TTTATCGGAG TTGCAGTTGC

2601 GCCCGCGAAC GACATTTATA ATGAACGTGA ATTGCTCAAC AGTATGAACA

2651 TTTCGCAGCC TACCGTAGTG TTTGTTTCCA AAAAGGGGTT GCAAAAAATT

Fig. 6

```
2701  TTGAACGTGC AAAAAAAATT ACCAATAATC CAGAAAATTA TTATCATGGA
2751  TTCTAAAACG GATTACCAGG GATTTCAGTC GATGTACACG TTCGTCACAT
2801  CTCATCTACC TCCCGGTTTT AATGAATACG ATTTTGTACC AGAGTCCTTT
2851  GATCGTGACA AAACAATTGC ACTGATAATG AATTCCTCTG GATCTACTGG
2901  GTTACCTAAG GGTGTGGCCC TTCCGCATAG AACTGCCTGC GTCAGATTCT
2951  CGCATGCCAG AGATCCTATT TTTGGCAATC AAATCATTCC GGATACTGCG
3001  ATTTTAAGTG TTGTTCCATT CCATCACGGT TTTGGAATGT TTACTACACT
3051  CGGATATTTG ATATGTGGAT TTCGAGTCGT CTTAATGTAT AGATTTGAAG
3101  AAGAGCTGTT TTTACGATCC CTTCAGGATT ACAAAATTCA AAGTGCGTTG
3151  CTAGTACCAA CCCTATTTTC ATTCTTCGCC AAAAGCACTC TGATTGACAA
3201  ATACGATTTA TCTAATTTAC ACGAAATTGC TTCTGGGGGC GCACCTCTTT
3251  CGAAAGAAGT CGGGGAAGCG GTTGCAAAAC GCTTCCATCT TCCAGGGATA
3301  CGACAAGGAT ATGGGCTCAC TGAGACTACA TCAGCTATTC TGATTACACC
3351  CGAGGGGGAT GATAAACCGG GCGCGGTCGG TAAAGTTGTT CCATTTTTTG
3401  AAGCGAAGGT TGTGGATCTG GATACCGGGA AAACGCTGGG CGTTAATCAG
3451  AGAGGCGAAT TATGTGTCAG AGGACCTATG ATTATGTCCG GTTATGTAAA
3501  CAATCCGGAA GCGACCAACG CCTTGATTGA CAAGGATGGA TGGCTACATT
3551  CTGGAGACAT AGCTTACTGG GACGAAGACG AACACTTCTT CATAGTTGAC
3601  CGCTTGAAGT CTTTAATTAA ATACAAAGGA TATCAGGTGG CCCCCGCTGA
3651  ATTGGAATCG ATATTGTTAC AACACCCCAA CATCTTCGAC GCGGGCGTGG
3701  CAGGTCTTCC CGACGATGAC GCCGGTGAAC TTCCCGCCGC CGTTGTTGTT
3751  TTGGAGCACG GAAAGACGAT GACGGAAAAA GAGATCGTGG ATTACGTCGC
3801  CAGTCAAGTA ACAACCGCGA AAAAGTTGCG CGGAGGAGTT GTGTTTGTGG
3851  ACGAAGTACC GAAAGGTCTT ACCGGAAAAC TCGACGCAAG AAAAATCAGA
3901  GAGATCCTCA TAAAGGCCAA GAAGGGCGGA AAGTCCAAAT TGTAAAATGT
3951  AACTGTATTC AGCGATGACG AAATTCTTAG CTATTGTAAT GACTCTAGAG
4001  GATCTTTGTG AAGGAACCTT ACTTCTGTGG TGTGACATAA TTGGACAAAC
4051  TACCTACAGA GATTTAAAGC TCTAAGGTAA ATATAAAATT TTTAAGTGTA
```

Fig. 6

4101 TAATGTGTTA AACTACTGAT TCTAATTGTT TGTGTATTTT AGATTCCAAC

4151 CTATGGAACT GATGAATGGG AGCAGTGGTG GAATGCCTTT AATGAGGAAA

4201 ACCTGTTTTG CTCAGAAGAA ATGCCATCTA GTGATGATGA GGCTACTGCT

4251 GACTCTCAAC ATTCTACTCC TCCAAAAAAG AAGAGAAAGG TAGAAGACCC

4301 CAAGGACTTT CCTTCAGAAT TGCTAAGTTT TTTGAGTCAT GCTGTGTTTA

4351 GTAATAGAAC TCTTGCTTGC TTTGCTATTT ACACCACAAA GGAAAAAGCT

4401 GCACTGCTAT ACAAGAAAAT TATGGAAAAA TATTCTGTAA CCTTTATAAG

4451 TAGGCATAAC AGTTATAATC ATAACATACT GTTTTTTCTT ACTCCACACA

4501 GGCATAGAGT GTCTGCTATT AATAACTATG CTCAAAAATT GTGTACCTTT

4551 AGCTTTTTAA TTTGTAAAGG GGTTAATAAG GAATATTTGA TGTATAGTGC

4601 CTTGACTAGA GATCATAATC AGCCATACCA CATTTGTAGA GGTTTTACTT

4651 GCTTTAAAAA ACCTCCCACA CCTCCCCCTG AACCTGAAAC ATAAAATGAA

4701 TGCAATTGTT GTTGTTAACT TGTTTATTGC AGCTTATAAT GGTTACAAAT

4751 AAAGCAATAG CATCACAAAT TTCACAAATA AAGCATTTTT TTCACTGCAT

4801 TCTAGTTGTG GTTTGTCCAA ACTCATCAAT GTATCTTATC ATGTCTGGAT

4851 CCCCGGGTCC CTATAGTGAG TCGTATTAGC TTGGCGTAAT CATGGTCATA

4901 GCTGTTTCCT GTGTGAAATT GTTATCCGCT CACAATTCCA CACAACATAC

4951 GAGCCGGAAG CATAAAGTGT AAAGCCTGGG GTGCCTAATG AGTGAGCTAA

5001 CTCACATTAA TTGCGTTGCG CTCACTGCCC GCTTTCCAGT CGGGAAACCT

5051 GTCGTGCCAG CTGCATTAAT GAATCGGCCA ACGCGCGGGG AGAGGCGGTT

5101 TGCGTATTGG GCGCTCTTCC GCTTCCTCGC TCACTGACTC GCTGCGCTCG

5151 GTCGTTCGGC TGCGGCGAGC GGTATCAGCT CACTCAAAGG CGGTAATACG

5201 GTTATCCACA GAATCAGGGG ATAACGCAGG AAAGAACATG TGAGCAAAAG

5251 GCCAGCAAAA GGCCAGGAAC CGTAAAAAGG CCGCGTTGCT GGCGTTTTTC

5301 CATAGGCTCC GCCCCCCTGA CGAGCATCAC AAAAATCGAC GCTCAAGTCA

5351 GAGGTGGCGA AACCCGACAG GACTATAAAG ATACCAGGCG TTTCCCCCTG

5401 GAAGCTCCCT CGTGCGCTCT CCTGTTCCGA CCCTGCCGCT TACCGGATAC

5451 CTGTCCGCCT TTCTCCCTTC GGGAAGCGTG GCGCTTTCTC AATGCTCACG

Fig. 6

5501 CTGTAGGTAT CTCAGTTCGG TGTAGGTCGT TCGCTCCAAG CTGGGCTGTG

5551 TGCACGAACC CCCCGTTCAG CCCGACCGCT GCGCCTTATC CGGTAACTAT

5601 CGTCTTGAGT CCAACCCGGT AAGACACGAC TTATCGCCAC TGGCAGCAGC

5651 CACTGGTAAC AGGATTAGCA GAGCGAGGTA TGTAGGCGGT GCTACAGAGT

5701 TCTTGAAGTG GTGGCCTAAC TACGGCTACA CTAGAAGGAC AGTATTTGGT

5751 ATCTGCGCTC TGCTGAAGCC AGTTACCTTC GGAAAAAGAG TTGGTAGCTC

5801 TTGATCCGGC AAACAAACCA CCGCTGGTAG CGGTGGTTTT TTTGTTTGCA

5851 AGCAGCAGAT TACGCGCAGA AAAAAAGGAT CTCAAGAAGA TCCTTTGATC

5901 TTTTCTACGG GGTCTGACGC TCAGTGGAAC GAAAACTCAC GTTAAGGGAT

5951 TTTGGTCATG AGATTATCAA AAAGGATCTT CACCTAGATC CTTTTAAATT

6001 AAAAATGAAG TTTTAAATCA ATCTAAAGTA TATATGAGTA AACTTGGTCT

6051 GACAGTTACC AATGCTTAAT CAGTGAGGCA CCTATCTCAG CGATCTGTCT

6101 ATTTCGTTCA TCCATAGTTG CCTGACTCCC CGTCGTGTAG ATAACTACGA

6151 TACGGGAGGG CTTACCATCT GGCCCCAGTG CTGCAATGAT ACCGCGAGAC

6201 CCACGCTCAC CGGCTCCAGA TTTATCAGCA ATAAACCAGC CAGCCGGAAG

6251 GGCCGAGCGC AGAAGTGGTC CTGCAACTTT ATCCGCCTCC ATCCAGTCTA

6301 TTAATTGTTG CCGGGAAGCT AGAGTAAGTA GTTCGCCAGT TAATAGTTTG

6351 CGCAACGTTG TTGCCATTGC TACAGGCATC GTGGTGTCAC GCTCGTCGTT

6401 TGGTATGGCT TCATTCAGCT CCGGTTCCCA ACGATCAAGG CGAGTTACAT

6451 GATCCCCCAT GTTGTGCAAA AAAGCGGTTA GCTCCTTCGG TCCTCCGATC

6501 GTTGTCAGAA GTAAGTTGGC CGCAGTGTTA TCACTCATGG TTATGGCAGC

6551 ACTGCATAAT TCTCTTACTG TCATGCCATC CGTAAGATGC TTTTCTGTGA

6601 CTGGTGAGTA CTCAACCAAG TCATTCTGAG AATAGTGTAT GCGGCGACCG

6651 AGTTGCTCTT GCCCGGCGTC AATACGGGAT AATACCGCGC CACATAGCAG

6701 AACTTTAAAA GTGCTCATCA TTGGAAAACG TTCTTCGGGG CGAAAACTCT

6751 CAAGGATCTT ACCGCTGTTG AGATCCAGTT CGATGTAACC CACTCGTGCA

6801 CCCAACTGAT CTTCAGCATC TTTTACTTTC ACCAGCGTTT CTGGGTGAGC

6851 AAAAACAGGA AGGCAAAATG CCGCAAAAAA GGGAATAAGG GCGACACGGA

Fig. 6

```
6901  AATGTTGAAT ACTCATACTC TTCCTTTTTC AATATTATTG AAGCATTTAT
6951  CAGGGTTATT GTCTCATGAG CGGATACATA TTTGAATGTA TTTAGAAAAA
7001  TAAACAAATA GGGGTTCCGC GCACATTTCC CCGAAAAGTG CCACCTGACG
7051  TCTAAGAAAC CATTATTATC ATGACATTAA CCTATAAAAA TAGGCGTATC
7101  ACGAGGCCCT TTCGTCTCGC GCGTTTCGGT GATGACGGTG AAAACCTCTG
7151  ACACATGCAG CTCCCGGAGA CGGTCACAGC TTGTCTGTAA GCGGATGCCG
7201  GGAGCAGACA AGCCCGTCAG GGCGCGTCAG CGGGTGTTGG CGGGTGTCGG
7251  GGCTGGCTTA ACTATGCGGC ATCAGAGCAG ATTGTACTGA GAGTGCACCA
7301  TATGCGGTGT GAAATACCGC ACAGATGCGT AAGGAGAAAA TACCGCATCA
7351  GGCGCCATTC GCCATTCAGG CTGCGCAACT GTTGGGAAGG GCGATCGGTG
7401  CGGGCCTCTT CGCTATTACG CCAGCTGGCG AAAGGGGGAT GTGCTGCAAG
7451  GCGATTAAGT TGGGTAACGC CAGGGTTTTC CCAGTCACGA CGTTGTAAAA
7501  CGACGGCCAG TGAATTTCGA CCTGCAGtcg actttttta tatatacagg
7551  aggccgag
```

Fig. 6

JCVPshort-hgdnf Length: 6565 June 8, 1999 16:57 Type: N Check:

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   1  GCTAGCCATT TAGGTGACAC TATAGAATAG ATCCCCATGA AGTTATGGGA
  51  TGTCGTGGCT GTCTGCCTGG TGCTGCTCCA CACCGCGTCC GCCTTCCCGC
 101  TGCCCGCCGG TAAGAGGCCT CCCGAGGCGC CCGCCGAAGA CCGCTCCCTC
 151  GGCCGCCGCC GCGCGCCCTT CGCGCTGAGC AGTGACTCAA ATATGCCAGA
 201  GGATTATCCT GATCAGTTCG ATGATGTCAT GGATTTTATT CAAGCCACCA
 251  TTAAAAGACT GAAAAGGTCA CCAGATAAAC AAATGGCAGT GCTTCCTAGA
 301  AGAGAGCGGA ATCGGCAGGC TGCAGCTGCC AACCCAGAGA ATTCCAGAGG
 351  AAAAGGTCGG AGAGGCCAGA GGGGCAAAAA CCGGGGTTGT GTCTTAACTG
 401  CAATACATTT AAATGTCACT GACTTGGGTC TGGGCTATGA AACCAAGGAG
 451  GAACTGATTT TTAGGTACTG CAGCGGCTCT TGCGATGCAG CTGAGACAAC
 501  GTACGACAAA ATATTGAAAA ACTTATCCAG AAATAGAAGG CTGGTGAGTG
 551  ACAAAGTAGG GCAGGCATGT TGCAGACCCA TCGCCTTTGA TGATGACCTG
 601  TCGTTTTTAG ATGATAACCT GGTTTACCAT ATTCTAAGAA AGCATTCCGC
 651  TAAAAGGTGT GGATGTATCT GACTGGTGCG CCGTCTTTCC CGACGTTAAA
 701  GGGATGAAAC CACAAGACTT ACCTTCGCTC GGAAGTAAAA CGACAAACAC
 751  ACACAGTTTT GCCCGTTTTC ATGAGAAATG GGACGTCTGC GCACGAAACG
 801  CGCCGTCGCT TGAGGAGGAC TTGTACAAAC ACGATCTATG CAGGTTTCCC
 851  CAACTGACAC AAACCGTGCA ACTTGAAACT CCGCCTGGTC TTTCCAGGTC
 901  TAGAGGGGTA ACATTTTGTA CTGTGTTTGA CTCCACGCTC GATCCACTAG
 951  CGAGTGTTAG TAGCGGTACT GCTGTCTCGT AGCGGAGCAT GTTGGCCGTG
1001  GGAACACCTC CTTGGTAACA AGGACCCACG GGGCCGAAAG CCATGTCCTA
1051  ACGGACCCAA CATGTGTGCA ACCCCAGCAC GGCAGCTTTA CTGTGAAACC
1101  CACTTCAAGG TGACATTGAT ACTGGTACTC AAACACTGGT GACAGGCTAA
1151  GGATGCCCTT CAGGTACCCC GAGGTAACAA GCGACACTCG GGATCTGAGA
1201  AGGGGACTGG GACTTCTTTA AAGTGCCCAG TTTAAAAAGC TTCTACGCCT
1251  GAATAGGTGA CCGGAGGCCG GCACCTTTCC TTTTATAACC ACTGAACACA
1301  TGGAAGACGC CAAAAACATA AAGAAAGGCC CGGCGCCATT CTATCCTCTA
1351  GAGGATGGAA CCGCTGGAGA GCAACTGCAT AAGGCTATGA AGAGATACGC
1401  CCTGGTTCCT GGAACAATTG CTTTTACAGA TGCACATATC GAGGTGAACA
1451  TCACGTACGC GGAATACTTC GAAATGTCCG TTCGGTTGGC AGAAGCTATG
1501  AAACGATATG GGCTGAATAC AAATCACAGA ATCGTCGTAT GCAGTGAAAA
1551  CTCTCTTCAA TTCTTTATGC CGGTGTTGGG CGCGTTATTT ATCGGAGTTG
1601  CAGTTGCGCC CGCGAACGAC ATTTATAATG AACGTGAATT GCTCAACAGT
1651  ATGAACATTT CGCAGCCTAC CGTAGTGTTT GTTTCCAAAA AGGGGTTGCA
1701  AAAAATTTTG AACGTGCAAA AAAAATTACC AATAATCCAG AAAATTATTA
1751  TCATGGATTC TAAAACGGAT TACCAGGGAT TTCAGTCGAT GTACACGTTC
1801  GTCACATCTC ATCTACCTCC CGGTTTTAAT GAATACGATT TTGTACCAGA
1851  GTCCTTTGAT CGTGACAAAA CAATTGCACT GATAATGAAT TCCTCTGGAT
1901  CTACTGGGTT ACCTAAGGGT GTGGCCCTTC CGCATAGAAC TGCCTGCGTC
1951  AGATTCTCGC ATGCCAGAGA TCCTATTTTT GGCAATCAAA TCATTCCGGA
2001  TACTGCGATT TTAAGTGTTG TTCCATTCCA TCACGGTTTT GGAATGTTTA
2051  CTACACTCGG ATATTTGATA TGTGGATTTC GAGTCGTCTT AATGTATAGA
2101  TTTGAAGAAG AGCTGTTTTT ACGATCCCTT CAGGATTACA AAATTCAAAG
2151  TGCGTTGCTA GTACCAACCC TATTTTCATT CTTCGCCAAA AGCACTCTGA
2201  TTGACAAATA CGATTTATCT AATTTACACG AAATTGCTTC TGGGGGCGCA
2251  CCTCTTTCGA AAGAAGTCGG GGAAGCGGTT GCAAAACGCT TCCATCTTCC
2301  AGGGATACGA CAAGGATATG GGCTCACTGA GACTACATCA GCTATTCTGA
2351  TTACACCCGA GGGGGATGAT AAACCGGGCG CGGTCGGTAA AGTTGTTCCA
2401  TTTTTTGAAG CGAAGGTTGT GGATCTGGAT ACCGGGAAAA CGCTGGGCGT
2451  TAATCAGAGA GGCGAATTAT GTGTCAGAGG ACCTATGATT ATGTCCGGTT
2501  ATGTAAACAA TCCGGAAGCG ACCAACGCCT TGATTGACAA GGATGGATGG
2551  CTACATTCTG GAGACATAGC TTACTGGGAC GAAGACGAAC ACTTCTTCAT
2601  AGTTGACCGC TTGAAGTCTT TAATTAAATA CAAAGGATAT CAGGTGGCCC
2651  CCGCTGAATT GGAATCGATA TTGTTACAAC ACCCCAACAT CTTCGACGCG
2701  GGCGTGGCAG GTCTTCCCGA CGATGACGCC GGTGAACTTC CCGCCGCCGT
2751  TGTTGTTTTG GAGCACGGAA AGACGATGAC GGAAAAAGAG ATCGTGGATT
2801  ACGTCGCCAG TCAAGTAACA ACCGCGAAAA AGTTGCGCGG AGGAGTTGTG
2851  TTTGTGGACG AAGTACCGAA AGGTCTTACC GGAAAACTCG ACGCAAGAAA
2901  AATCAGAGAG ATCCTCATAA AGGCCAAGAA GGGCGGAAAG TCCAAATTGT
2951  AAAATGTAAC TGTATTCAGC GATGACGAAA TTCTTAGCTA TTGTAATGAC
3001  TCTAGAGGAT CTTTGTGAAG GAACCTTACT TCTGTGGTGT GACATAATTG
3051  GACAAACTAC CTACAGAGAT TTAAAGCTCT AAGGTAAATA TAAAATTTTT
3101  AAGTGTATAA TGTGTTAAAC TACTGATTCT AATTGTTTGT GTATTTTAGA
3151  TTCCAACCTA TGGAACTGAT GAATGGGAGC AGTGGTGGAA TGCCTTTAAT
```

Fig. 7

```
3201  GAGGAAAACC TGTTTTGCTC AGAAGAAATG CCATCTAGTG ATGATGAGGC
3251  TACTGCTGAC TCTCAACATT CTACTCCTCC AAAAAAGAAG AGAAAGGTAG
3301  AAGACCCCAA GGACTTTCCT TCAGAATTGC TAAGTTTTTT GAGTCATGCT
3351  GTGTTTAGTA ATAGAACTCT TGCTTGCTTT GCTATTTACA CCACAAAGGA
3401  AAAAGCTGCA CTGCTATACA AGAAAATTAT GGAAAAATAT TCTGTAACCT
3451  TTATAAGTAG GCATAACAGT TATAATCATA ACATACTGTT TTTTCTTACT
3501  CCACACAGGC ATAGAGTGTC TGCTATTAAT AACTATGCTC AAAAATTGTG
3551  TACCTTTAGC TTTTTAATTT GTAAAGGGGT TAATAAGGAA TATTTGATGT
3601  ATAGTGCCTT GACTAGAGAT CATAATCAGC CATACCACAT TTGTAGAGGT
3651  TTTACTTGCT TTAAAAAACC TCCCACACCT CCCCCTGAAC CTGAAACATA
3701  AAATGAATGC AATTGTTGTT GTTAACTTGT TTATTGCAGC TTATAATGGT
3751  TACAAATAAA GCAATAGCAT CACAAATTTC ACAAATAAAG CATTTTTTTC
3801  ACTGCATTCT AGTTGTGGTT TGTCCAAACT CATCAATGTA TCTTATCATG
3851  TCTGGATCCC CGGGTCCCTA TAGTGAGTCG TATTAGCTTG GCGTAATCAT
3901  GGTCATAGCT GTTTCCTGTG TGAAATTGTT ATCCGCTCAC AATTCCACAC
3951  AACATACGAG CCGGAAGCAT AAAGTGTAAA GCCTGGGGTG CCTAATGAGT
4001  GAGCTAACTC ACATTAATTG CGTTGCGCTC ACTGCCCGCT TTCCAGTCGG
4051  GAAACCTGTC GTGCCAGCTG CATTAATGAA TCGGCCAACG CGCGGGGAGA
4101  GGCGGTTTGC GTATTGGGCG CTCTTCCGCT TCCTCGCTCA CTGACTCGCT
4151  GCGCTCGGTC GTTCGGCTGC GGCGAGCGGT ATCAGCTCAC TCAAAGGCGG
4201  TAATACGGTT ATCCACAGAA TCAGGGGATA ACGCAGGAAA GAACATGTGA
4251  GCAAAAGGCC AGCAAAAGGC CAGGAACCGT AAAAAGGCCG CGTTGCTGGC
4301  GTTTTTCCAT AGGCTCCGCC CCCCTGACGA GCATCACAAA AATCGACGCT
4351  CAAGTCAGAG GTGGCGAAAC CCGACAGGAC TATAAAGATA CCAGGCGTTT
4401  CCCCCTGGAA GCTCCCTCGT GCGCTCTCCT GTTCCGACCC TGCCGCTTAC
4451  CGGATACCTG TCCGCCTTTC TCCCTTCGGG AAGCGTGGCG CTTTCTCAAT
4501  GCTCACGCTG TAGGTATCTC AGTTCGGTGT AGGTCGTTCG CTCCAAGCTG
4551  GGCTGTGTGC ACGAACCCCC CGTTCAGCCC GACCGCTGCG CCTTATCCGG
4601  TAACTATCGT CTTGAGTCCA ACCCGGTAAG ACACGACTTA TCGCCACTGG
4651  CAGCAGCCAC TGGTAACAGG ATTAGCAGAG CGAGGTATGT AGGCGGTGCT
4701  ACAGAGTTCT TGAAGTGGTG GCCTAACTAC GGCTACACTA GAAGGACAGT
4751  ATTTGGTATC TGCGCTCTGC TGAAGCCAGT TACCTTCGGA AAAAGAGTTG
4801  GTAGCTCTTG ATCCGGCAAA CAAACCACCG CTGGTAGCGG TGGTTTTTTT
4851  GTTTGCAAGC AGCAGATTAC GCGCAGAAAA AAAGGATCTC AAGAAGATCC
4901  TTTGATCTTT TCTACGGGGT CTGACGCTCA GTGGAACGAA AACTCACGTT
4951  AAGGGATTTT GGTCATGAGA TTATCAAAAA GGATCTTCAC CTAGATCCTT
5001  TTAAATTAAA AATGAAGTTT TAAATCAATC TAAAGTATAT ATGAGTAAAC
5051  TTGGTCTGAC AGTTACCAAT GCTTAATCAG TGAGGCACCT ATCTCAGCGA
5101  TCTGTCTATT TCGTTCATCC ATAGTTGCCT GACTCCCCGT CGTGTAGATA
5151  ACTACGATAC GGGAGGGCTT ACCATCTGGC CCCAGTGCTG CAATGATACC
5201  GCGAGACCCA CGCTCACCGG CTCCAGATTT ATCAGCAATA AACCAGCCAG
5251  CCGGAAGGGC CGAGCGCAGA AGTGGTCCTG CAACTTTATC CGCCTCCATC
5301  CAGTCTATTA ATTGTTGCCG GGAAGCTAGA GTAAGTAGTT CGCCAGTTAA
5351  TAGTTTGCGC AACGTTGTTG CCATTGCTAC AGGCATCGTG GTGTCACGCT
5401  CGTCGTTTGG TATGGCTTCA TTCAGCTCCG GTTCCCAACG ATCAAGGCGA
5451  GTTACATGAT CCCCCATGTT GTGCAAAAAA GCGGTTAGCT CCTTCGGTCC
5501  TCCGATCGTT GTCAGAAGTA AGTTGGCCGC AGTGTTATCA CTCATGGTTA
5551  TGGCAGCACT GCATAATTCT CTTACTGTCA TGCCATCCGT AAGATGCTTT
5601  TCTGTGACTG GTGAGTACTC AACCAAGTCA TTCTGAGAAT AGTGTATGCG
5651  GCGACCGAGT TGCTCTTGCC CGGCGTCAAT ACGGGATAAT ACCGCGCCAC
5701  ATAGCAGAAC TTTAAAAGTG CTCATCATTG GAAAACGTTC TTCGGGGCGA
5751  AAACTCTCAA GGATCTTACC GCTGTTGAGA TCCAGTTCGA TGTAACCCAC
5801  TCGTGCACCC AACTGATCTT CAGCATCTTT TACTTTCACC AGCGTTTCTG
5851  GGTGAGCAAA AACAGGAAGG CAAAATGCCG CAAAAAAGGG AATAAGGGCG
5901  ACACGGAAAT GTTGAATACT CATACTCTTC CTTTTTCAAT ATTATTGAAG
5951  CATTTATCAG GGTTATTGTC TCATGAGCGG ATACATATTT GAATGTATTT
6001  AGAAAAATAA ACAAATAGGG GTTCCGCGCA CATTTCCCCG AAAAGTGCCA
6051  CCTGACGTCT AAGAAACCAT TATTATCATG ACATTAACCT ATAAAAATAG
6101  GCGTATCACG AGGCCCTTTC GTCTCGCGCG TTTCGGTGAT GACGGTGAAA
6151  ACCTCTGACA CATGCAGCTC CCGGAGACGG TCACAGCTTG TCTGTAAGCG
6201  GATGCCGGGA GCAGACAAGC CCGTCAGGGC GCGTCAGCGG GTGTTGGCGG
6251  GTGTCGGGGC TGGCTTAACT ATGCGGCATC AGAGCAGATT GTACTGAGAG
6301  TGCACCATAT GCGGTGTGAA ATACCGCACA GATGCGTAAG GAGAAAATAC
6351  CGCATCAGGC GCCATTCGCC ATTCAGGCTG CGCAACTGTT GGGAAGGGCG
6401  ATCGGTGCGG GCCTCTTCGC TATTACGCCA GCTGGCGAAA GGGGGATGTG
6451  CTGCAAGGCG ATTAAGTTGG GTAACGCCAG GGTTTTCCCA GTCACGACGT
6501  TGTAAAACGA CGGCCAGTGA ATTTCGACCT GCAGtcgact ttttttatat
```

Fig. 7

6551 atacaggagg ccgag

Fig. 7

pRetroOFF-E6E7 Length: 7840 June 10, 1999 12:21 Type: N Check: 5234

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   1 TCGAGTTTAC CACTCCCTAT CAGTGATAGA GAAAAGTGAA AGTCGAGTTT
  51 ACCACTCCCT ATCAGTGATA GAGAAAAGTG AAAGTCGAGT TTACCACTCC
 101 CTATCAGTGA TAGAGAAAGT GAAAGTCGAG TTTACCACTC CCTATCAGTG
 151 ATAGAGAAAA GTGAAAGTCG AGTTTACCAC TCCCTATCAG TGATAGAGAA
 201 AAGTGAAAGT CGAGTTTACC ACTCCCTATC AGTGATAGAG AAAAGTGAAG
 251 TCGAGTTTAC CACTCCCTAT CAGTGATAGA GAAAAGTGAA AGTCGAGCTC
 301 GGTACCCGGG TCGAGTAGGC GTGTACGGTG GGAGGCCTAT ATAAGCAGAG
 351 CTCGTTTAGT GAACCGTCAG ATCGCCTGGA GACGCCATCC ACGCTGTTTT
 401 GACCTCCATA GAAGACACCG GGACCGATCC AGCCTgcggc cgcagatcta
 451 attcaccggt tagtataaaa gcagacattt tatgcaccaa aagagaactg
 501 caatgtttca ggacccacag gagcgaccca gaaagttacc acagttatgc
 551 acagagctgc aaacaactat acatgatata atattagaat gtgtgtactg
 601 caagcaacag ttactgcgac gtgaggtata tgactttgct tttcgggatt
 651 tatgcatagt atatagagat gggaatccat atgctgtatg tgataaatgt
 701 ttaaagtttt attctaaaat tagtgagtat agacattatt gttatagttt
 751 gtatggaaca acattagaac agcaatacaa caaaccgttg tgtgatttgt
 801 taattaggtg tattaactgt caaaagccac tgtgtcctga agaaaagcaa
 851 agacatctgg acaaaaagca aagattccat aatataaggg gtcggtggac
 901 cggtcgatgt atgtcttgtt gcagatcatc aagaacacgt agagaaaccc
 951 agctgtaatc atgcatggag atacacctac attgcatgaa tatatgttag
1001 atttgcaacc agagacaact gatctctact gttatgagca attaaatgac
1051 agctcagagg aggaggatga aatagatggt ccagctggac aagcagaacc
1101 ggacagagcc cattacaata ttgtaacctt ttgttgcaag tgtgactcta
1151 cgcttcggtt gtgcgtacaa agcacacacg tagacattcg tactttggaa
1201 gacctgttaa tyggcacact aggaattgtg tgccccatct gttctcagaa
1251 accataatct accatggctg atcctgcagg atccCCCGGG AACAACAACA
1301 ATTGCATTCA TTTTATGTTT CAGGTTCAGG GGGAGGTGTG GGAGGTTTTT
1351 TAAAGCAAGT AAAACCTCTA CAAATGTGGT ATGGCTGATT ATGATCCTGC
1401 AAGCCTCGTC GTCTGGCCGG ACCACGCTAT CTGTGCAAGG TCCCCGGACG
1451 CGCGCTCCAT GAGCAGAGCG TCGCGCCCCC TACCCACCGT ACTCGTCAAT
1501 TCCAAGGGCA TCGGTAAACA GAGCGCCGTA GGGGGCGGAG TCGTGGGGGG
1551 TAAATCCCGG ACCCGGGGAA TCCCCGTCCC CCAACATGTC CAGATCGAAA
1601 TCGTCTAGCG CGTCGGCATG CGCCATCGCC ACGTCCTCGC CGTATAAGTG
1651 GAGCTCGTCC CCCAGGCTGA CATCGGTCGG GGGGGCCGTC GACAGTCTGC
1701 GCGTGTGTCC GCGGGGAGAA AGGACAGGCG CGGAGCCGCC AGCCCCGCCT
1751 CTTCGGGGGC GTCGTCGTCC GGGAGATCGA GCAGGCCCTC GATGGTAGAC
1801 CCGTAATTGT TTTTCGTACG CGCGCGGCTG TACGCGGACC CACTTTCACA
1851 TTTAAGTTGT TTTTCTAATC CGCATATGAT CAATTCAAGG CCGAATAAGA
1901 AGGCTGGCTC TGCACCTTGG TGATCAAATA ATTCGATAGC TTGTCGTAAT
1951 AATGGCGGCA TACTATCAGT AGTAGGTGTT TCCCTTTCTT CTTTAGCGAC
2001 TTGATGCTCT TGATCTTCCA ATACGCAACC TAAAGTAAAA TGCCCCACAG
2051 CGCTGAGTGC ATATAATGCA TTCTCTAGTG AAAAACCTTG TTGGCATAAA
2101 AAGGCTAATT GATTTTCGAG AGTTTCATAC TGTTTTTCTG TAGGCCGTGT
2151 ACCTAAATGT ACTTTTGCTC CATCGCGATG ACTTAGTAAA GCACATCTAA
2201 AACTTTTAGC GTTATTACGT AAAAAATCTT GCCAGCTTTC CCCTTCTAAA
2251 GGGCAAAAGT GAGTATGGTG CCTATCTAAC ATCTCAATGG CTAAGGCGTC
2301 GAGCAAAGCC CGCTTATTTT TTACATGCCA ATACAATGTA GGCTGCTCTA
2351 CACCTAGCTT CTGGGCGAGT TTACGGGTTG TTAAACCTTC GATTCCGACC
2401 TCATTAAGCA GCTCTAATGC GCTGTTAATC ACTTTACTTT TATCTAATCT
2451 AGACATGGTG GAAGCTTTTT GCAAAAGCCT AGGCCTCCAA AAAAGCCTCC
2501 TCACTACTTC TGGAATAGCT CAGAGGCCGA GGCGGCCTCG GCCTCTGCAT
2551 AAATAAAAAA AATTAGTCAG CCATGGGGCG GAGAATGGGC GGAACTGGGC
2601 GGAGTTAGGG GCGGGATGGG CGGAGTTAGG GGCGGGACTA TGGTTGCTGA
2651 CTAATTGAGA TGCATGCTTT GCATACTTCT GCCTGCTGGG GAGCCTGGGG
2701 ACTTTCCACA CCTGGTTGCT GACTAATTGA GATGCATGCT TTGCATACTT
2751 CTGCCTGCTG GGGAGCCTGG GGACTTTCCA CACCCTAACT GACACACATT
2801 CCACAGGTCG ACTAGATCGA ATTCTCAATT GTTTTACGCG GCCCGATGCA
2851 TGGGGTCGTG CGCTCCTTTC GGTCGGGCGC TGCGGGTCGT GGGGCGGGCG
2901 TCAGGCACCG GGCTTGCGGG TCATGCACCA GGTCGCGCGG TCCTTCGGGC
2951 ACTCGACGTC GGCGGTGACG GTGAAGCCGA GCCGCTCGTA GAAGGGGAGG
3001 TTGCGGGGCG CGGAGGTCTC CAGGAAGGCG GGCACCCCGG CGCGCTCGGC
3051 CGCCTCCACT CCGGGGAGCA CGACGGCGCT GCCCAGACCC TTGCCCTGGT
3101 GGTCGGGCGA GACGCCGACG GTGGCCAGGA ACCACGCGGG CTCCTTGGGC
3151 CGGTGCGGCG CCAGGAGGCC TTCCATCTGT TGCTGCGCGG CCAGCCGGGA
```

Fig. 8

```
3201  ACCGCTCAAC TCGGCCATGC GCGGGCCGAT CTCGGCGAAC ACCGCCCCCG
3251  CTTCGACGCT CTCCGGCGTG GTCCAGACCG CCACCGCGGC GCCGTCGTCC
3301  GCGACCCACA CCTTGCCGAT GTCGAGCCCG ACGCGCGTGA GGAAGAGTTC
3351  TTGCAGCTCG GTGACCCGCT CGATGTGGCG GTCCGGATCG ACGGTGTGGC
3401  GCGTGGCGGG GTAGTCGGCG AACGCGGCGG CGAGGGTGCG TACGGCCCTG
3451  GGGACGTCGT CGCGGGTGGC GAGGCGCACC GTGGGCTTGT ACTCGGTCAT
3501  GGTAAGCTGA TCCGGCCGGC GCCTAGAGAA GGAGTGAGGG CTGGATAAAG
3551  GGAGGATTGA GGCGGGGTCG AAAGAGGAGG TTCAAGGGGG AGAGACGGCG
3601  CGGATGGAAG AAGAGGAGGC GGAGGCTTAG GGTGTACAAA GGGCTTGACC
3651  CAGGGAGGGG GGTCAAAAGC CAAGGCTTCC CAGGTCACGA TGTAGGGGAC
3701  CTGGTCTGGG TGTCCATGCG GGCCAGGTGA AAAGACCTTG ATCTTAACCT
3751  GGGTGATGAC GTCTCGGTTA AAGGTGCCGT CTCGCGGCCA TCCGACGTTA
3801  AAGGTTGGCC ATTCTGCAGA GCAGAAGGTA ACCCAACGTC TCTTCTTGAC
3851  ATCTACCGAC TGGTTGTGAG CGAGCCGCTC GACATCTTTC CAGTGATCTA
3901  AGGTCAAACT TAAGGGAGTG GTAACAGTCT GGCCCTAATT TTCAGACAAA
3951  TACAGAAACA CAGTCAGACA GAGACAACAC AGAACGATGC TGCAGCAGAC
4001  AAGACGCGCG GCTTCGGTTC CAAACCGAAA GCAAAAATTC AGACGGAGGC
4051  GGGAACTGTT TTAGGTTCTC GTCTCCTACC AGAACCACAT ATCCTGACGG
4101  GGTCGGATTC CACATCGACT CCCTTCCTCA GGTCGGGCCA CAAAAACGGC
4151  CCCCAAAGTC CCTGGGACGT CTCCCAGGGT TGCGGCCGGG TGTTCAGAAC
4201  TCGTCAGTTC CACCACGGGT CCGCCAGATA CAGAGCTAGT TAGCTAACTA
4251  GTACCGACGC AGGCGCATAA AATCAGTCAT AGACACTAGA CAATCGGACA
4301  GACACAGATA AGTTGCTGGC CAGCTTACCT CCCGGTGGTG GGTCGGTGGT
4351  CCCTGGGCAG GGGTCTCCCG ATCCCGGACG AGCCCCCAAA TGAAAGACCC
4401  CCGCTGACGG GTAGTCAATC ACTCAGAGGA GACCCTCCCA AGGAACAGCG
4451  AGACCACAAG TCGGATGCAA CTGCAAGAGG GTTTATTGGA TACACGGGTA
4501  CCCGGGCGAC TCAGTCAATC GGAGGACTGG CGCCCCGAGT GAGGGGTTGT
4551  GGGCTCTTTT ATTGAGCTCG GGGAGCAGAA GCGCGCGAAC AGAAGCGAGA
4601  AGCGAACTGA TTGGTTAGTT CAAATAAGGC ACAGGGTCAT TTCAGGTCCT
4651  TGGGGCACCC TGGAAACATC TGATGGTTCT CTAGAAACTG CTGAGGGCTG
4701  GACCGCATCT GGGGACCATC TGTTCTTGGC CCTGAGCCGG GGCAGGAACT
4751  GCTTACCACA GATATCCTGT TTGGCCCATA TTCAGCTGTT CCATCTGTTC
4801  TTGGCCCTGA GCCGGGGCAG GAACTGCTTA CCACAGATAT CCTGTTTGGC
4851  CCATATTCAG GCTGCAGGTG GCACTTTTCG GGGAAATGTG CGCGGAACCC
4901  CTATTTGTTT ATTTTTCTAA ATACATTCAA ATATGTATCC GCTCATGAGA
4951  CAATAACCCT GATAAATGCT TCAATAATAT TGAAAAAGGA AGAGTATGAG
5001  TATTCAACAT TTCCGTGTCG CCCTTATTCC CTTTTTTGCG GCATTTTGCC
5051  TTCCTGTTTT TGCTCACCCA GAAACGCTGG TGAAAGTAAA AGATGCTGAA
5101  GATCAGTTGG GTGCACGAGT GGGTTACATC GAACTGGATC TCAACAGCGG
5151  TAAGATCCTT GAGAGTTTTC GCCCCGAAGA ACGTTTTCCA ATGATGAGCA
5201  CTTTTAAAGT TCTGCTATGT GGCGCGGTAT TATCCCGTGT TGACGCCGGG
5251  CAAGAGCAAC TCGGTCGCCG CATACACTAT TCTCAGAATG ACTTGGTTGA
5301  GTACTCACCA GTCACAGAAA AGCATCTTAC GGATGGCATG ACAGTAAGAG
5351  AATTATGCAG TGCTGCCATA ACCATGAGTG ATAACACTGC GGCCAACTTA
5401  CTTCTGACAA CGATCGGAGG ACCGAAGGAG CTAACCGCTT TTTTGCACAA
5451  CATGGGGGAT CATGTAACTC GCCTTGATCG TTGGGAACCG GAGCTGAATG
5501  AAGCCATACC AAACGACGAG CGTGACACCA CGATGCCTGT AGCAATGGCA
5551  ACAACGTTGC GCAAACTATT AACTGGCGAA CTACTTACTC TAGCTTCCCG
5601  GCAACAATTA ATAGACTGGA TGGAGGCGGA TAAAGTTGCA GGACCACTTC
5651  TGCGCTCGGC CCTTCCGGCT GGCTGGTTTA TTGCTGATAA ATCTGGAGCC
5701  GGTGAGCGTG GGTCTCGCGG TATCATTGCA GCACTGGGGC CAGATGGTAA
5751  GCCCTCCCGT ATCGTAGTTA TCTACACGAC GGGGAGTCAG GCAACTATGG
5801  ATGAACGAAA TAGACAGATC GCTGAGATAG GTGCCTCACT GATTAAGCAT
5851  TGGTAACTGT CAGACCAAGT TTACTCATAT ATACTTTAGA TTGATTTGCG
5901  GCCGGCCGCA AACTTCATTT TTAATTTAAA AGGATCTAGG TGAAGATCCT
5951  TTTTGATAAT CTCATGACCA AAATCCCTTA ACGTGAGTTT TCGTTCCACT
6001  GAGCGTCAGA CCCCGTAGAA AAGATCAAAG GATCTTCTTG AGATCCTTTT
6051  TTTCTGCGCG TAATCTGCTG CTTGCAAACA AAAAAACCAC CGCTACCAGC
6101  GGTGGTTTGT TTGCCGGATC AAGAGCTACC AACTCTTTTT CCGAAGGTAA
6151  CTGGCTTCAG CAGAGCGCAG ATACCAAATA CTGTCCTTCT AGTGTAGCCG
6201  TAGTTAGGCC ACCACTTCAA GAACTCTGTA GCACCGCCTA CATACCTCGC
6251  TCTGCTAATC CTGTTACCAG TGGCTGCTGC CAGTGGCGAT AAGTCGTGTC
6301  TTACCGGGTT GGACTCAAGA CGATAGTTAC CGGATAAGGC GCAGCGGTCG
6351  GGCTGAACGG GGGGTTCGTG CACACAGCCC AGCTTGGAGC GAACGACCTA
6401  CACCGAACTG AGATACCTAC AGCGTGAGCT ATGAGAAAGC GCCACGCTTC
6451  CCGAAGGGAG AAAGGCGGAC AGGTATCCGG TAAGCGGCAG GGTCGGAACA
6501  GGAGAGCGCA CGAGGGAGCT TCCAGGGGGA AACGCCTGGT ATCTTTATAG
```

Fig. 8

```
6551  TCCTGTCGGG TTTCGCCACC TCTGACTTGA GCGTCGATTT TTGTGATGCT
6601  CGTCAGGGGG GCGGAGCCTA TGGAAAAACG CCAGCAACGC GGCCTTTTTA
6651  CGGTTCCTGG CCTTTTGCTG GCCTTTTGCT CACATGTTCT TTCCTGCGTT
6701  ATCCCCTGAT TCTGTGGATA ACCGTATTAC CGCCTTTGAG TGAGCTGATA
6751  CCGCTCGCCG CAGCCGAACG ACCGAGCGCA GCGAGTCAGT GAGCGAGGAA
6801  GCGGAAGAGC GCCAATACGC AAACCGCCTC TCCCCGCGCG TTGGCCGATT
6851  CATTAATGCA ACTATGGCCA TTTAATGTAA ATACTTAAGA AAAAAAACCA
6901  AATTAATTTT GATACATGCT GCATGTGAAG ACCCCCGCTG ACGGGTAGTC
6951  AATCACTCAG AGGAGACCCT CCCAAGGCAG CGAGACCACA AGTCGGAAAT
7001  GAAAGACCCC CGCTGACGGG TAGTCAATCA CTCAGAGGAG ACCCTCCCAA
7051  GGAACAGCGA GACCACAAGT CGGATGCAAC TGCAAGAGGG TTTATTGGAT
7101  ACACGGGTAC CCGGGCGACT CAGTCAATCG GAGGACTGGC GCCCCGAGTG
7151  AGGGGTTGTG GGCTCTTTTA TTGAGCTCGG GGAGCAGAAG CGCGCGAACA
7201  GAAGCGAGAA GCGAACTGAT TGGTTAGTTC AAATAAGGCA CAGGGTCATT
7251  TCAGGTCCTT GGGGCACCCT GGAAACATCT GATGGTTCTC TAGAAACTGC
7301  TGAGGGCTGG ACCGCATCTG GGGACCATCT GTTCTTGGCC CTGAGCCGGG
7351  GCAGGAACTG CTTACCACAG ATATCCTGTT TGGCCCATAT TCAGCTGTTC
7401  CATCTGTTCT TGGCCCTGAG CCGGGGCAGG AACTGCTTAC CACAGATATC
7451  CTGTTTGGCC CATATTCAGC TGTTCCATCT GTTCCTGACC TTGATCTGAA
7501  CTTCTCTATT CTCAGTTATG TATTTTTCCA TGCCTTGCAA AATGGCGTTA
7551  CTTAAGCTAG CAGATCTGCT AGCTTGCCAA ACCTACAGGT GGGGTCTTTC
7601  ATTCCCCCCT TTTTCTGGAG ACTAAATAAA ATCTTTTATT TTATGCGCAC
7651  ATTTCCCCGA AAAGTGCCAC CTGACGTCTA AGAAACCATT ATTATCATGA
7701  CATTAACCTA TAAAAATAGG CGTATCACGA GGCCCTTTCG TCCGCACATT
7751  TCCCCGAAAA GTGCCACCTG ACGTCTAAGA AACCATTATT ATCATGACAT
7801  TAACCTATAA AAATAGGCGT ATCACGAGGC CCTTTCGTCC
```

Fig. 8

pRetroOPP-U19tsa58 Length: 8852

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   1  TCGAGTTTAC CACTCCCTAT CAGTGATAGA GAAAAGTGAA AGTCGAGTTT
  51  ACCACTCCCT ATCAGTGATA GAGAAAAGTG AAAGTCGAGT TTACCACTCC
 101  CTATCAGTGA TAGAGAAAGT GAAAGTCGAG TTTACCACTC CCTATCAGTG
 151  ATAGAGAAAA GTGAAAGTCG AGTTTACCAC TCCCTATCAG TGATAGAGAA
 201  AAGTGAAAGT CGAGTTTACC ACTCCCTATC AGTGATAGAG AAAAGTGAAG
 251  TCGAGTTTAC CACTCCCTAT CAGTGATAGA GAAAAGTGAA AGTCGAGCTC
 301  GGTACCCGGG TCGAGTAGGC GTGTACGGTG GGAGGCCTAT ATAAGCAGAG
 351  CTCGTTTAGT GAACCGTCAG ATCGCCTGGA GACGCCATCC ACGCTGTTTT
 401  GACCTCCATA GAAGACACCG GGACCGATCC AGCCTGCGGC CGCTTAATTA
 451  AGTTTAAACG GATCCxxxxx xxxxxxatgc catctagtga tgatgaggct
 501  actgctgact ctcaacattc tactcctcca aaaaagaaga gaaaggtaga
 551  agacccccaag gactttcctt cagaattgct aagtttttttg agtcatgctg
 601  tgtttagtaa tagaactctt gcttgctttg ctatttacac cacaaaggaa
 651  aaagctgcac tgctatacaa gaaaattatg gaaaaatatt ctgtaacctt
 701  tataagtagg cataacagtt ataatcataa catactgttt tttcttactc
 751  cacacaggca tagagtgtct gctattaata actatgctca aaaattgtgt
 801  acctttagct ttttaatttg taaaggggtt aataaggaat atttgatgta
 851  tagtgccttg actagagatc catttttctgt tattgaggaa agtttgccag
 901  gtgggttaaa ggagcatgat tttaatccag aagaagcaga ggaaactaaa
 951  caagtgtcct ggaagcttgt aacagagtat gcaatggaaa caaaatgtga
1001  tgatgtgttg ttattgcttg ggatgtactt ggaatttcag tacagttttg
1051  aaatgtgttt aaaatgtatt aaaaaagaac agcccagcca ctataagtac
1101  catgaaaagc attatgcaaa tgctgctata tttgctgaca gcaaaaacca
1151  aaaaaccata tgccaacagg ctgttgatac tgttttagct aaaaagcggg
1201  ttgatagcct acaattaact agagaacaaa tgttaacaaa cagatttaat
1251  gatcttttgg ataggatgga tataatgttt ggttctacag gctctgctga
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1351  aaatggattc agtggtgtat gacttttttaa aatgcatggt gtacaacatt
1401  cctaaaaaaa gatactggct gtttaaagga ccaattgata gtggtaaaac
1451  tacattagca gctgctttgc ttgaattatg tgggggggaaa gctttaaatg
1501  ttaatttgcc cttggacagg ctgaactttg agctaggagt agctattgac
1551  cagtttttag tagtttttga ggatgtaaag ggcactggag gggagtccag
1601  agatttgcct tcaggtcagg gaattaataa cctggacaat ttaagggatt
1651  atttggatgg cagtgttaag gtaaacttag aaaagaaaca cctaaataaa
1701  agaactcaaa tatttccccc tggaatagtc accatgaatg agtacagtgt
1751  gcctaaaaca ctgcaggcca gatttgtaaa acaaatagat tttaggccca
1801  aagattattt aaagcattgc ctggaacgca gtgagttttt gttagaaaag
1851  agaataattc aaagtggcat tgctttgctt cttatgttaa tttggtacag
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2151  tcccaaggct catttcaggc ccctcagtcc tcacagtctg ttcatgatca
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2301  GGAACAACAA CAATTGCATT CATTTTATGT TTCAGGTTCA GGGGGAGGTG
2351  TGGGAGGTTT TTTAAAGCAA GTAAAACCTC TACAAATGTG GTATGGCTGA
2401  TTATGATCCT GCAAGCCTCG TCGTCTGGCC GGACCACGCT ATCTGTGCAA
2451  GGTCCCCGGA CGCGCCCTCC ATGAGCAGAG CGTCGCGCCC CCTACCCACC
2501  GTACTCGTCA ATTCCAAGGG CATCGGTAAA CAGAGCGCCG TAGGGGGCGG
2551  AGTCGTGGGG GGTAAATCCC GGACCCGGGG AATCCCCGTC CCCCAACATG
2601  TCCAGATCGA AATCGTCTAG CGCGTCGGCA TGCGCCATCG CCACGTCCTC
2651  GCCGTATAAG TGGAGCTCGT CCCCCAGGCT GACATCGGTC GGGGGGGCCG
2701  TCGACAGTCT GCGCGTGTGT CCGCGGGGAG AAAGGACAGG CGCGGAGCCG
2751  CCAGCCCCGC CTCTTCGGGG GCGTCGTCGT CCGGGAGATC GAGCAGGCCC
2801  TCGATGGTAG ACCCGTAATT GTTTTTCGTA CGCGCGCGGC TGTACGCGGA
2851  CCCACTTTCA CATTTAAGTT GTTTTTCTAA TCCGCATATG ATCAATTCAA
2901  GGCCGAATAA GAAGGCTGGC TCTGCACCTT GGTGATCAAA TAATTCGATA
2951  GCTTGTCGTA ATAATGGCGG CATACTATCA GTAGTAGGTG TTTCCCTTTC
3001  TTCTTTAGCG ACTTGATGCT CTTGATCTTC CAATACGCAA CCTAAAGTAA
3051  AATGCCCCAC AGCGCTGAGT GCATATAATG CATTCTCTAG TGAAAAACCT
3101  TGTTGGCATA AAAAGGCTAA TTGATTTTCG AGAGTTTCAT ACTGTTTTTC
3151  TGTAGGCCGT GTACCTAAAT GTACTTTTGC TCCATCGCGA TGACTTAGTA
3201  AAGCACATCT AAAACTTTTA GCGTTATTAC GTAAAAAATC TTGCCAGCTT
```

Fig. 9

3251 TCCCCTTCTA AAGGGCAAAA GTGAGTATGG TGCCTATCTA ACATCTCAAT
3301 GGCTAAGGCG TCGAGCAAAG CCCGCTTATT TTTTACATGC CAATACAATG
3351 TAGGCTGCTC TACACCTAGC TTCTGGGCGA GTTTACGGGT TGTTAAACCT
3401 TCGATTCCGA CCTCATTAAG CAGCTCTAAT GCGCTGTTAA TCACTTTACT
3451 TTTATCTAAT CTAGACATGG TGGAAGCTTT TTGCAAAAGC CTAGGCCTCC
3501 AAAAAAGCCT CCTCACTACT TCTGGAATAG CTCAGAGGCC GAGGCGGCCT
3551 CGGCCTCTGC ATAAATAAAA AAAATTAGTC AGCCATGGGG CGGAGAATGG
3601 GCGGAACTGG GCGGAGTTAG GGGCGGGATG GGCGGAGTTA GGGGCGGGAC
3651 TATGGTTGCT GACTAATTGA GATGCATGCT TTGCATACTT CTGCCTGCTG
3701 GGGAGCCTGG GGACTTTCCA CACCTGGTTG CTGACTAATT GAGATGCATG
3751 CTTTGCATAC TTCTGCCTGC TGGGGAGCCT GGGGACTTTC CACACCCTAA
3801 CTGACACACA TTCCACAGGT CGACTAGATC GAATTCTCAA TTGTTTTACG
3851 CGGCCCGATG CATGGGGTCG TGCGCTCCTT TCGGTCGGGC GCTGCGGGTC
3901 GTGGGGCGGG CGTCAGGCAC CGGGCTTGCG GGTCATGCAC CAGGTCGCGC
3951 GGTCCTTCGG GCACTCGACG TCGGCGGTGA CGGTGAAGCC GAGCCGCTCG
4001 TAGAAGGGGA GGTTGCGGGG CGCGGAGGTC TCCAGGAAGG CGGGCACCCC
4051 GGCGCGCTCG GCCGCCTCCA CTCCGGGGAG CACGACGGCG CTGCCCAGAC
4101 CCTTGCCCTG GTGGTCGGGC GAGACGCCGA CGGTGGCCAG GAACCACGCG
4151 GGCTCCTTGG GCCGGTGCGG CGCCAGGAGG CCTTCCATCT GTTGCTGCGC
4201 GGCCAGCCGG GAACCGCTCA ACTCGGCCAT GCGCGGGCCG ATCTCGGCGA
4251 ACACCGCCCC CGCTTCGACG CTCTCCGGCG TGGTCCAGAC CGCCACCGCG
4301 GCGCCGTCGT CCGCGACCCA CACCTTGCCG ATGTCGAGCC CGACGCGCGT
4351 GAGGAAGAGT TCTTGCAGCT CGGTGACCCG CTCGATGTGG CGGTCCGGAT
4401 CGACGGTGTG GCGCGTGGCG GGGTAGTCGG CGAACGCGGC GGCGAGGGTG
4451 CGTACGGCCC TGGGGACGTC GTCGCGGGTG GCGAGGCGCA CCGTGGGCTT
4501 GTACTCGGTC ATGGTAAGCT GATCCGGCCG GCGCCTAGAG AAGGAGTGAG
4551 GGCTGGATAA AGGGAGGATT GAGGCGGGGT CGAAAGAGGA GGTTCAAGGG
4601 GGAGAGACGG CGCGGATGGA AGAAGAGGAG GCGGAGGCTT AGGGTGTACA
4651 AAGGGCTTGA CCCAGGGAGG GGGGTCAAAA GCCAAGGCTT CCCAGGTCAC
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4751 TGATCTTAAC CTGGGTGATG AGGTCTCGGT TAAAGGTGCC GTCTCGCGGC
4801 CATCCGACGT TAAAGGTTGG CCATTCTGCA GAGCAGAAGG TAACCCAACG
4851 TCTCTTCTTG ACATCTACCG ACTGGTTGTG AGCGAGCCGC TCGACATCTT
4901 TCCAGTGATC TAAGGTCAAA CTTAAGGGAG TGGTAACAGT CTGGCCCTAA
4951 TTTTCAGACA AATACAGAAA CACAGTCAGA CAGAGACAAC ACAGAACGAT
5001 GCTGCAGCAG ACAAGACGCG CGGCTTCGGT TCCAAACCGA AAGCAAAAAT
5051 TCAGACGGAG GCGGGAACTG TTTTAGGTTC TCGTCTCCTA CCAGAACCAC
5101 ATATCCTGAC GGGGTCGGAT TCCACATCGA CTCCCTTCCT CAGGTCGGGC
5151 CACAAAAACG GCCCCCAAAG TCCCTGGGAC GTCTCCCAGG GTTGCGGCCG
5201 GGTGTTCAGA ACTCGTCAGT TCCACCACGG GTCCGCCAGA TACAGAGCTA
5251 GTTAGCTAAC TAGTACCGAC GCAGGCGCAT AAAATCAGTC ATAGACACTA
5301 GACAATCGGA CAGACACAGA TAAGTTGCTG GCCAGCTTAC CTCCCGGTGG
5351 TGGGTCGGTG GTCCCTGGGC AGGGGTCTCC CGATCCCGGA CGAGCCCCCA
5401 AATGAAAGAC CCCCGCTGAC GGGTAGTCAA TCACTCAGAG GAGACCCTCC
5451 CAAGGAACAG CGAGACCACA AGTCGGATGC AACTGCAAGA GGGTTTATTG
5501 GATACACGGG TACCCGGGCG ACTCAGTCAA TCGGAGGACT GGCGCCCCGA
5551 GTGAGGGGTT GTGGGCTCTT TTATTGAGCT CGGGGAGCAG AAGCGCGCGA
5601 ACAGAAGCGA GAAGCGAACT GATTGGTTAG TTCAAATAAG GCACAGGGTC
5651 ATTTCAGGTC CTTGGGGCAC CCTGGAAACA TCTGATGGTT CTCTAGAAAC
5701 TGCTGAGGGC TGGACCGCAT CTGGGGACCA TCTGTTCTTG GCCCTGAGCC
5751 GGGGCAGGAA CTGCTTACCA CAGATATCCT GTTTGGCCCA TATTCAGCTG
5801 TTCCATCTGT TCTTGGCCCT GAGCCGGGGC AGGAACTGCT TACCACAGAT
5851 ATCCTGTTTG GCCCATATTC AGGCTGCAGG TGGCACTTTT CGGGGAAATG
5901 TGCGCGGAAC CCCTATTTGT TTATTTTTCT AAATACATTC AAATATGTAT
5951 CCGCTCATGA GACAATAACC CTGATAAATG CTTCAATAAT ATTGAAAAAG
6001 GAAGAGTATG AGTATTCAAC ATTTCCGTGT CGCCCTTATT CCCTTTTTTG
6051 CGGCATTTTG CCTTCCTGTT TTTGCTCACC CAGAAACGCT GGTGAAAGTA
6101 AAAGATGCTG AAGATCAGTT GGGTGCACGA GTGGGTTACA TCGAACTGGA
6151 TCTCAACAGC GGTAAGATCC TTGAGAGTTT TCGCCCCGAA GAACGTTTTC
6201 CAATGATGAG CACTTTTAAA GTTCTGCTAT GTGGCGCGGT ATTATCCCGT
6251 GTTGACGCCG GGCAAGAGCA ACTCGGTCGC CGCATACACT ATTCTCAGAA
6301 TGACTTGGTT GAGTACTCAC CAGTCACAGA AAAGCATCTT ACGGATGGCA
6351 TGACAGTAAG AGAATTATGC AGTGCTGCCA TAACCATGAG TGATAACACT
6401 GCGGCCAACT TACTTCTGAC AACGATCGGA GGACCGAAGG AGCTAACCGC
6451 TTTTTTGCAC AACATGGGGG ATCATGTAAC TCGCCTTGAT CGTTGGGAAC
6501 CGGAGCTGAA TGAAGCCATA CCAAACGACG AGCGTGACAC CACGATGCCT
6551 GTAGCAATGG CAACAACGTT GCGCAAACTA TTAACTGGCG AACTACTTAC

Fig. 9

```
6601  TCTAGCTTCC CGGCAACAAT TAATAGACTG GATGGAGGCG GATAAAGTTG
6651  CAGGACCACT TCTGCGCTCG GCCCTTCCGG CTGGCTGGTT TATTGCTGAT
6701  AAATCTGGAG CCGGTGAGCG TGGGTCTCGC GGTATCATTG CAGCACTGGG
6751  GCCAGATGGT AAGCCCTCCC GTATCGTAGT TATCTACACG ACGGGGAGTC
6801  AGGCAACTAT GGATGAACGA AATAGACAGA TCGCTGAGAT AGGTGCCTCA
6851  CTGATTAAGC ATTGGTAACT GTCAGACCAA GTTTACTCAT ATATACTTTA
6901  GATTGATTTG CGGCCGGCCG CAAACTTCAT TTTTAATTTA AAAGGATCTA
6951  GGTGAAGATC CTTTTTGATA ATCTCATGAC CAAAATCCCT TAACGTGAGT
7001  TTTCGTTCCA CTGAGCGTCA GACCCCGTAG AAAAGATCAA AGGATCTTCT
7051  TGAGATCCTT TTTTTCTGCG CGTAATCTGC TGCTTGCAAA CAAAAAAACC
7101  ACCGCTACCA GCGGTGGTTT GTTTGCCGGA TCAAGAGCTA CCAACTCTTT
7151  TTCCGAAGGT AACTGGCTTC AGCAGAGCGC AGATACCAAA TACTGTCCTT
7201  CTAGTGTAGC CGTAGTTAGG CCACCACTTC AAGAACTCTG TAGCACCGCC
7251  TACATACCTC GCTCTGCTAA TCCTGTTACC AGTGGCTGCT GCCAGTGGCG
7301  ATAAGTCGTG TCTTACCGGG TTGGACTCAA GACGATAGTT ACCGGATAAG
7351  GCGCAGCGGT CGGGCTGAAC GGGGGGTTCG TGCACACAGC CCAGCTTGGA
7401  GCGAACGACC TACACCGAAC TGAGATACCT ACAGCGTGAG CTATGAGAAA
7451  GCGCCACGCT TCCCGAAGGG AGAAAGGCGG ACAGGTATCC GGTAAGCGGC
7501  AGGGTCGGAA CAGGAGAGCG CACGAGGGAG CTTCCAGGGG GAAACGCCTG
7551  GTATCTTTAT AGTCCTGTCG GGTTTCGCCA CCTCTGACTT GAGCGTCGAT
7601  TTTTGTGATG CTCGTCAGGG GGGCGGAGCC TATGGAAAAA CGCCAGCAAC
7651  GCGGCCTTTT TACGGTTCCT GGCCTTTTGC TGGCCTTTTG CTCACATGTT
7701  CTTTCCTGCG TTATCCCCTG ATTCTGTGGA TAACCGTATT ACCGCCTTTG
7751  AGTGAGCTGA TACCGCTCGC CGCAGCCGAA CGACCGAGCG CAGCGAGTCA
7801  GTGAGCGAGG AAGCGGAAGA GCGCCAATAC GCAAACCGCC TCTCCCCGCG
7851  CGTTGGCCGA TTCATTAATG CAACTATGGC CATTTAATGT AAATACTTAA
7901  GAAAAAAAAC CAAATTAATT TTGATACATG CTGCATGTGA AGACCCCCGC
7951  TGACGGGTAG TCAATCACTC AGAGGAGACC CTCCCAAGGC AGCGAGACCA
8001  CAAGTCGGAA ATGAAAGACC CCCGCTGACG GGTAGTCAAT CACTCAGAGG
8051  AGACCCTCCC AAGGAACAGC GAGACCACAA GTCGGATGCA ACTGCAAGAG
8101  GGTTTATTGG ATACACGGGT ACCCGGGCGA CTCAGTCAAT CGGAGGACTG
8151  GCGCCCCGAG TGAGGGGTTG TGGGCTCTTT TATTGAGCTC GGGGAGCAGA
8201  AGCGCGCGAA CAGAAGCGAG AAGCGAACTG ATTGGTTAGT TCAAATAAGG
8251  CACAGGGTCA TTTCAGGTCC TTGGGGCACC CTGGAAACAT CTGATGGTTC
8301  TCTAGAAACT GCTGAGGGCT GGACCGCATC TGGGGACCAT CTGTTCTTGG
8351  CCCTGAGCCG GGGCAGGAAC TGCTTACCAC AGATATCCTG TTTGGCCCAT
8401  ATTCAGCTGT TCCATCTGTT CTTGGCCCTG AGCCGGGGCA GGAACTGCTT
8451  ACCACAGATA TCCTGTTTGG CCCATATTCA GCTGTTCCAT CTGTTCCTGA
8501  CCTTGATCTG AACTTCTCTA TTCTCAGTTA TGTATTTTTC CATGCCTTGC
8551  AAAATGGCGT TACTTAAGCT AGCAGATCTG CTAGCTTGCC AAACCTACAG
8601  GTGGGGTCTT TCATTCCCCC CTTTTTCTGG AGACTAAATA AAATCTTTTA
8651  TTTTATGCGC ACATTTCCCC GAAAAGTGCC ACCTGACGTC TAAGAAACCA
8701  TTATTATCAT GACATTAACC TATAAAAATA GGCGTATCAC GAGGCCCTTT
8751  CGTCCGCACA TTTCCCCGAA AAGTGCCACC TGACGTCTAA GAAACCATTA
8801  TTATCATGAC ATTAACCTAT AAAAATAGGC GTATCACGAG GCCCTTTCGT
8851  CC
```

Fig. 9

puhd10-3-hIL3 Length: 3621

```
   1  ctcgagtttа ccactcccta tcagtgatag agaaaagtga aagtcgagtt
  51  taccactccc tatcagtgat agagaaaagt gaaagtcgag tttaccactc
 101  cctatcagtg atagaga aa gtgaaagtcg agtttaccac tccctatcag
 151  tgatagagaa aagtgaaagt cgagtttacc actccctatc agtgatagag
 201  aaaagtgaaa gtcgagttta ccactcccta tcagtgatag agaaaagtga
 251  aagtcgagtt taccactccc tatcagtgat agagaaaagt gaaagtcgag
 301  ctcggtaccc gggtcgagta ggcgtgtacg gtgggaggcc tatataagca
 351  gagctcgttt agtgaaccgt cagatcgcct ggagacgcca tccacgctgt
 401  tttgacctcc atagaagaca ccgggaccga tccagcctcc gcggccccga
 451  attaaacagt cgagctacgt caacgaaaaa taaaatccaa acatgagccg
 501  cctgcccgtc ctgctcctgc tccaactcct ggtccgcccc ggactccaag
 551  ctcccatgac ccagacaacg tccttgaaga caagctgggt taactgctct
 601  aacatgatcg atgaaattat aacacactta aagcagccac ctttgccttt
 651  gctggacttc aacaacctca atggggaaga ccaagacatt ctgatggaaa
 701  ataaccttcg aaggccaaac ctggaggcat tcaacagggc tgtcaagagt
 751  ttacagaacg catcagcaat tgagagcatt cttaaaaatc tcctgccatg
 801  tctgcccctg gccacggccg cacccacgcg acatccaatc catatcaagg
 851  acggtgactg gaatgaattc cggaggaaac tgacgttcta tctgaaaacc
 901  cttgagaatg cgcaggctca acagacgact ttgagcctcg cgatctttta
 951  gaactcgact ctagacatga taagatacat tgatgagttt ggacaaacca
1001  caactagaat gcagtgaaaa aaatgctttа tttgtgaaat ttgtgatgct
1051  attgctttat ttgtaaccat tataagctgc aataaacaag ttaacaacaa
1101  caattgcatt cattttatgt ttcaggttca gggggaggtg tgggaggttt
1151  tttaaagcaa gtaaaacctc tacaaatgtg gtatggctga ttatgatcct
1201  gcaagcctcg tcgtctggcc ggaccacgct atctgtgcaa ggtccccgga
1251  cgcgcgctcc atgagcagag cgcccgccgc cgaggcaaga ctcgggcggc
1301  gccctgcccg tcccaccagg tcaacaggcg gtaaccggcc tcttcatcgg
1351  gaatgcgcgc gaccttcagc atcgccggca tgtcccctgg cggacgggaa
1401  gtatcagctc gaccaagctt ggcgagattt tcaggagcta aggaagctaa
1451  aatggagaaa aaaatcactg gatataccac cgttgatata tcccaatggc
1501  atcgtaaaga acattttgag gcatttcagt cagttgctca atgtacctat
1551  aaccagaccg ttcagctgca ttaatgaatc ggccaacgcg cggggagagg
1601  cggtttgcgt attgggcgct cttccgcttc ctcgctcact gactcgctgc
1651  gctcggtcgt tcggctgcgg cgagcggtat cagctcactc aaagtcggta
1701  atacggttat ccacagaatc aggggataac gcaggaaaga acatgtgagc
1751  aaaaggccag caaaaggcca ggaaccgtaa aaaggccgcg ttgctggcgt
1801  ttttccatag gctccgcccc cctgacgagc atcacaaaaa tcgacgctca
1851  agtcagaggt ggcgaaaccc gacaggacta taaagatacc aggcgtttcc
1901  cccctggaagc tccctcgtgc gctctcctgt tccgaccctg ccgcttaccg
1951  gatacctgtc cgcctttctc ccttcgggaa gcgtggcgct ttctcaatgc
2001  tcacgctgta ggtatctcag ttcggtgtag gtcgttcgct ccaagctggg
2051  ctgtgtgcac gaaccccccg ttcagcccga ccgctgcgcc ttatccggta
2101  actatcgtct tgagtccaac ccggtaagac acgacttatc gccactggaa
2151  gcagccactg gtaacaggat tagcagagcg aggtatgtag gcggtgctac
2201  agagttcttg aagtggtggc ctaactacgg ctacactaga aggacagtat
2251  ttggtatctg cgctctgctg aagccagtta ccttcggaaa aagagttggt
2301  agctcttgat ccggcaaaca aaccaccgct ggtagcggtg gttttttgt
2351  ttgcaagcag cagattacgc gcagaaaaaa aggatctcaa gaagatcctt
2401  tgatcttttc tacggggtct gacgctcagt ggaacgaaaa ctcacgttaa
2451  gggattttgg tcatgagatt atcaaaaagg atcttcacct agatcctttt
2501  aaattaaaaa tgaagtttta aatcaatcta aagtatatat gagtaaacтt
2551  ggtctgacag ttaccaatgc ttaatcagtg aggcacctat ctcagcgatc
2601  tgtctatttc gttcatccat agttgcctga ctccccgtcg tgtagataac
2651  tacgatacgg gagggcttac catctggccc cagtgctgca atgataccgc
2701  gagacccacg ctcaccggct ccagatttat cagcaataaa ccagccagcc
2751  ggaagggccg agcgcagaag tggtcctgca actttatccg cctccatcca
2801  gtctattaat tgttgccggg aagctagagt aagtagttcg ccagttaata
2851  gtttgcgcaa cgttgttgcc attgctacag gcatcgtgtg gtcacgctcg
2901  tcgtttggta tggcttcatt cagctccggt tcccaacgat caaggcgagt
2951  tacatgatcc cccatgttgt gcaaaaaagc ggttagctcc ttcggtcctc
3001  cgatcgttgt cagaagtaag ttggccgcag tgttatcact catggttatg
3051  gcagcactgc ataattctct tactgtcatg ccatccgtaa gatgcttttc
3101  tgtgactggt gagtactcaa ccaagtcatt ctgagaatag tgtatgcggc
3151  gaccgagttg ctcttgcccg tcgtcaatac gggataatac cgcgccacat
3201  agcagaactt taaaagtgct catcattgga aaacgttctt cggggcgaaa
```

Fig. 10

```
3251  actctcaagg atcttaccgc tgttgagatc cagttcgatg taacccactc
3301  gtgcacccaa ctgatcttca gcatctttta ctttcaccag cgtttctggg
3351  tgagcaaaaa caggaaggca aaatgccgca aaaaagggaa taagggcgac
3401  acggaaatgt tgaatactca tactcttcct ttttcaatat tattgaagca
3451  tttatcaggg ttattgtctc atgagcggat acatatttga atgtatttag
3501  aaaaataaac aaatagggGT tccgcgcaca tttccccgaa aagtgccacc
3551  tgacgtctaa gaaaccatta ttatcatgac attaacctat aaaaataggc
3601  gtatcacgag gccctttcgt c
```

Fig. 10

pUHD10-3-hIL6
Length: 3752 June 22, 1999 10:32 Type: N Check: 8139 ..

```
   1  ctcgagtttg ccactcccta tcagtgatag agaaaagtga aagtcgagtt
  51  taccactccc tatcagtgat agagaaaagt gaaagtcgag tttaccactc
 101  cctatcagtg atagagaaaa gtgaaagtcg agtttaccac tccctatcag
 151  tgatagagaa aagtgaaagt cgagtttacc actccctatc agtgatagag
 201  aaaaagtgaaa gtcgagttta ccactcccta tcagtgatag agaaaagtga
 251  aagtcgagtt taccactccc tatcagtgat agagaaaagt gaaagtcgag
 301  ctcggtaccc gggtcgagta ggcgtgtacg gtgggaggcc tatataagca
 351  gagctcgttt agtgaaccgt cagatcgcct ggagacgcca tccacgctgt
 401  tttgacctcc atagaagaca ccgggaccga tccagcctcc gcggtggcgg
 451  ccgctctaga actagtggat ccccccagctt acctgccatg ccagtacccc
 501  caggagaaga ttccaaaagat gtagccgccc cacacagaca gccactcacc
 551  tcttcagaac gaattgacaa acaaattcgg tacatcctcg acggcatctc
 601  agccctgaga aaggagacat gtaacaagag taacatgtgt gaaagcagca
 651  aagaggcact ggcagaaaac aacctgaacc ttccaaagat ggctgaaaaa
 701  gatggatgct tccaatctgg attcaatgag gagacttgcc tggtgaaaat
 751  catcactggt cttttggagt ttgaggtata cctagagtac ctccagaaca
 801  gatttgagag tagtgaggaa caagccagag ctgtccagat gagtacaaaa
 851  gtcctgatcc agttcctgca gaaaaaggca aagaatctag atgcaataac
 901  cacccctgac ccaagccaca atgccagcct gctgacgaag ctgcaggcac
 951  agaaccagtg gctgcaggac atgacaactc atctcattct gcgcagcttt
1001  aaggagttcc tgcagtccag cctgagggct cttcggcaaa tgtagtaagg
1051  atccgaattc gagctcggta cccgggggatc ctctagagga tccagacatg
1101  ataagataca ttgatgagtt tggacaaacc acaactagaa tgcagtgaaa
1151  aaaatgcttt atttgtgaaa tttgtgatgc tattgctttа tttgtaacca
1201  ttataagctg caataaacaa gttaacaaca acaattgcat tcattttatg
1251  tttcaggttc agggggaggt gtgggaggtt ttttaaagca agtaaaacct
1301  ctacaaatgt ggtatggctg attatgatcc tgcaagcctc gtcgtctggc
1351  cggaccacgc tatctgtgca aggtccccgg acgcgcgctc catgagcaga
1401  gcgcccgccg ccgaggcaag actcgggcgg cgccctgccc gtcccaccag
1451  gtcaacaggc ggtaaccggc ctcttcatcg ggaatgcgcg cgaccttcag
1501  catcgccggc atgtcccctg gcggacggga agtatcagct cgaccaagct
1551  tggcgagatt ttcaggagct aaggaagcta aaatggagaa aaaaatcact
1601  ggatataccа ccgttgatat atcccaatgg catcgtaaag aacattttga
1651  ggcatttcag tcagttgctc aatgtacctа taaccagacc gttcagctgc
1701  attaatgaat cggccaacgc gcggggagag gcggtttgcg tattgggcgc
1751  tcttccgctt cctcgctcac tgactcgctg cgctcggtcg ttcggctgcg
1801  gcgagcggta tcagctcact caaagtcggt aatacggtta tccacagaat
1851  caggggataa cgcaggaaag aacatgtgag caaaaggcca gcaaaaggcc
1901  aggaaccgta aaaaggccgc gttgctggcg tttttccata ggctccgccc
1951  cctgacgag catcacaaaa atcgacgctc aagtcagagg tggcgaaacc
2001  cgacaggact ataaagatac caggcgtttc cccctggaag ctccctcgtg
2051  cgctctcctg ttccgaccct gccgcttacc ggatacctgt ccgccttttct
2101  cccttcggga agcgtggcgc tttctcaatg ctcacgctgt aggtatctca
2151  gttcggtgta ggtcgttcgc tccaagctgg gctgtgtgca cgaacccccc
2201  gttcagcccg accgctgcgc cttatccggt aactatcgtc ttgagtccaa
2251  cccggtaaga cacgacttat cgccactgga agcagccact ggtaacagga
2301  ttagcagagc gaggtatgta ggcggtgcta cagagttctt gaagtggtgg
2351  cctaactacg gctacactag aaggacagta tttggtatct gcgctctgct
2401  gaagccagtt accttcggaa aaagagttgg tagctcttga tccggcaaac
2451  aaaccaccgc tggtagcggt ggtttttttg tttgcaagca gcagattacg
2501  cgcagaaaaa aaggatctca agaagatcct ttgatctttt ctacggggtc
2551  tgacgctcag tggaacgaaa actcacgtta agggattttg gtcatgagat
2601  tatcaaaaag gatcttcacc tagatccttt taaattaaaa atgaagtttt
2651  aaatcaatct aaagtatata tgagtaaact tggtctgaca gttaccaatg
2701  cttaatcagt gaggcaccta tctcagcgat ctgtctattt cgttcatcca
2751  tagttgcctg actccccgtc gtgtagataa ctacgatacg ggagggctta
2801  ccatctggcc ccagtgctgc aatgataccg cgagacccac gctcaccggc
2851  tccagattta tcagcaataa accagccagc cggaagggcc gagcgcagaa
2901  gtggtcctgc aactttatcc gcctccatcc agtctattaa ttgttgccgg
2951  gaagctagag taagtagttc gccagttaat agtttgcgca acgttgttgc
3001  cattgctaca ggcatcgtgt ggtcacgctc gtcgtttggt atggcttcat
3051  tcagctccgg ttcccaacga tcaaggcgag ttacatgatc ccccatgttg
3101  tgcaaaaaag cggttagctc cttcggtcct ccgatcgttg tcagaagtaa
3151  gttggccgca gtgttatcac tcatggttat ggcagcactg cataattctc
```

Fig. 11

```
3201  ttactgtcat gccatccgta agatgctttt ctgtgactgg tgagtactca
3251  accaagtcat tctgagaata gtgtatgcgg cgaccgagtt gctcttgccc
3301  gtcgtcaata cgggataata ccgcgccaca tagcagaact ttaaaagtgc
3351  tcatcattgg aaaacgttct tcggggcgaa aactctcaag gatcttaccg
3401  ctgttgagat ccagttcgat gtaacccact cgtgcaccca actgatcttc
3451  agcatctttt actttcacca gcgtttctgg gtgagcaaaa acaggaaggc
3501  aaaatgccgc aaaaaagggg ataagggcga cacggaaatg ttgaatactc
3551  atactcttcc tttttcaata ttattgaagc atttatcagg gttattgtct
3601  catgagcgga tacatatttg aatgtattta gaaaaataaa caaatagggg
3651  ttccgcgcac atttccccga aaagtgccac ctgacgtcta agaaaccatt
3701  attatcatga cattaacctc taaaaatagg cgtatcacga ggcccttcg
3751  tc
```

Fig. 11

puhd10-3-tgf

```
    ctcgagtttaccactccctatcagtgatagagaaaagtgaaagtcgagtttaccactccc
  1 ---------+---------+---------+---------+---------+---------+ 60

    tatcagtgatagagaaaagtgaaagtcgagtttaccactccctatcagtgatagagaaaa
 61 ---------+---------+---------+---------+---------+---------+ 120

    gtgaaagtcgagtttaccactccctatcagtgatagagaaaagtgaaagtcgagtttacc
121 ---------+---------+---------+---------+---------+---------+ 180

    actccctatcagtgatagagaaaagtgaaagtcgagtttaccactccctatcagtgatag
181 ---------+---------+---------+---------+---------+---------+ 240

    agaaaagtgaaagtcgagtttaccactccctatcagtgatagagaaaagtgaaagtcgag
241 ---------+---------+---------+---------+---------+---------+ 300

    ctcggtacccgggtcgagtaggcgtgtacggtgggaggcctatataagcagagctcgttt
301 ---------+---------+---------+---------+---------+---------+ 360

    agtgaaccgtcagatcgcctggagacgccatccacgctgttttgacctccatagaagaca
361 ---------+---------+---------+---------+---------+---------+ 420

    ccgggaccgatccagcctccgcggccccgaattcctgcagcccATGCACTTGCAAAGGGC
421 ---------+---------+---------+---------+---------+---------+ 480

    TCTGGTAGTCCTGGCCCTGCTGAACTTGGCCACAATCAGCCTCTCTCTGTCCACTTGCAC
481 ---------+---------+---------+---------+---------+---------+ 540

    CACGTTGGACTTCGGCCACATCAAGAAGAAGAGGGTGGAAGCCATTAGGGGACAGATCTT
541 ---------+---------+---------+---------+---------+---------+ 600

    GAGCAAGCTCAGGCTCACCAGCCCCCCTGAGCCATCGGTGATGACCCACGTCCCCTATCA
601 ---------+---------+---------+---------+---------+---------+ 660

    GGTCCTGGCACTTTACAACAGCACCCGGGAGTTGCTGGAAGAGATGCACGGGGAGAGGGA
661 ---------+---------+---------+---------+---------+---------+ 720

    GGAAGGCTGCACTCAGGAGACCTCGGAGTCTGAGTACTATGCCAAAGAGATCCATAAATT
721 ---------+---------+---------+---------+---------+---------+ 780

    CGACATGATCCAGGGACTGGCGGAGCACAATGAACTGGCCGTCTGCCCCAAAGGAATTAC
781 ---------+---------+---------+---------+---------+---------+ 840

    CTCTAAGGTTTTTCGTTTCAATGTGTCCTCAGTGGAGAAAAATGGAACCAATCTGTTCCG
841 ---------+---------+---------+---------+---------+---------+ 900

    GCCAGAGTTCCGGGTCTTGCGGGTGCCCAACCCCAGCTCCAAGCGCACAGAGCAGAGAAT
901 ---------+---------+---------+---------+---------+---------+ 960

    TGAGCTCTTCCAGATACTTCGACCGGATGAGCACATAGCCAAGCAGCGCTACATAGGTGG
961 ---------+---------+---------+---------+---------+---------+ 1020

    CAAGAATCTGCCCACAAGGGGCACCGCTGAATGGCTGTCTTTCGATGTCACTGACACTGT
1021 ---------+---------+---------+---------+---------+---------+ 1080

    GCGCGAGTGGCTGTTGAGGAGAGAGTCCAACTTGGGTCTGGAAATCAGCATCCACTGTCC
1081 ---------+---------+---------+---------+---------+---------+ 1140

    ATGTCACACCTTTCAGCCCAATGGAGACATACTGGAAAATGTTCATGAGGTGATGGAAAT
1141 ---------+---------+---------+---------+---------+---------+ 1200

    CAAATTCAAAGGAGTGGACAATGAAGATGACCATGGCCGTGGAGACCTGGGGCGTCTCAA
1201 ---------+---------+---------+---------+---------+---------+ 1260

    GAAGCAAAAGGATCACCACAACCCACACCTGATCCTCATGATGATCCCCCCACACCGACT
1261 ---------+---------+---------+---------+---------+---------+ 1320
```

Fig. 12

```
                GGACAGCCCAGGCCAGGGCAGTCAGAGGAAGAAGAGGGCCCTGGACACCAATTACTGCTT
1321 ---------+---------+---------+---------+---------+---------+---------+ 1380

                CCGCAACCTGGAGGAGAACTGCTGTGTACGCCCCCTTTATATTGACTTCCGGCAGGATCT
1381 ---------+---------+---------+---------+---------+---------+---------+ 1440

                AGGCTGGAAATGGGTCCACGAACCTAAGGGTTACTATGCCAACTTCTGCTCAGGCCCTTG
1441 ---------+---------+---------+---------+---------+---------+---------+ 1500

                CCCATACCTCCGCAGCGCAGACACAACCCATAGCACGGTGCTTGGACTATACAACACCCT
1501 ---------+---------+---------+---------+---------+---------+---------+ 1560

                GAACCCAGAGGCGTCTGCCTCGCCATGCTGCGTCCCCCAGGACCTGGAGCCCCTGACCAT
1561 ---------+---------+---------+---------+---------+---------+---------+ 1620

                CTTGTACTATGTGGGCAGAACCCCCAAGGTGGAGCAGCTGTCCAACATGGTGGTGAAGTC
1621 ---------+---------+---------+---------+---------+---------+---------+ 1680

                GTGTAAGTGCAGCTGAgggggatccactagttctagaggatccagacatgataagatacа
1681 ---------+---------+---------+---------+---------+---------+---------+ 1740

                ttgatgagtttggacaaaccacaactagaatgcagtgaaaaaaatgctttatttgtgaaa
1741 ---------+---------+---------+---------+---------+---------+---------+ 1800

                tttgtgatgctattgctttatttgtaaccattataagctgcaataaacaagttaacaaca
1801 ---------+---------+---------+---------+---------+---------+---------+ 1860

                acaattgcattcattttatgtttcaggttcaggggggaggtgtgggaggtttttttaaagca
1861 ---------+---------+---------+---------+---------+---------+---------+ 1920

                agtaaaacctctacaaatgtggtatggctgattatgatcctgcaagcctcgtcgtctggc
1921 ---------+---------+---------+---------+---------+---------+---------+ 1980

                cggaccacgctatctgtgcaaggtccccggacgcgcgctccatgagcagagcgcccgccg
1981 ---------+---------+---------+---------+---------+---------+---------+ 2040

                ccgaggcaagactcgggcggcgccctgcccgtcccaccaggtcaacaggcggtaaccggc
2041 ---------+---------+---------+---------+---------+---------+---------+ 2100

                ctcttcatcgggaatgcgcgcgaccttcagcatcgccggcatgtcccctggcggacgggа
2101 ---------+---------+---------+---------+---------+---------+---------+ 2160

                agtatcagctcgaccaagcttggcgagattttcaggagctaaggaagctaaaatggagaa
2161 ---------+---------+---------+---------+---------+---------+---------+ 2220

                aaaaatcactggatataccaccgttgatatatcccaatggcatcgtaaagaacattttga
2221 ---------+---------+---------+---------+---------+---------+---------+ 2280

                ggcatttcagtcagttgctcaatgtacctataaccagaccgttcagctgcattaatgaat
2281 ---------+---------+---------+---------+---------+---------+---------+ 2340

                cggccaacgcgcggggagaggcggtttgcgtattgggcgctcttccgcttcctcgctcac
2341 ---------+---------+---------+---------+---------+---------+---------+ 2400

                tgactcgctgcgctcggtcgttcggctgcggcgagcggtatcagctcactcaaagtcggt
2401 ---------+---------+---------+---------+---------+---------+---------+ 2460

                aatacggttatccacagaatcaggggataacgcaggaaagaacatgtgagcaaaaggcca
2461 ---------+---------+---------+---------+---------+---------+---------+ 2520

                gcaaaaggccaggaaccgtaaaaaggccgcgttgctggcgtttttccataggctccgccc
2521 ---------+---------+---------+---------+---------+---------+---------+ 2580

                ccctgacgagcatcacaaaaatcgacgctcaagtcagaggtggcgaaacccgacaggact
2581 ---------+---------+---------+---------+---------+---------+---------+ 2640
```

Fig. 12

```
      ataaagataccaggcgtttccccctggaagctccctcgtgcgctctcctgttccgaccct
2641  ---------+---------+---------+---------+---------+---------+ 2700

      gccgcttaccggatacctgtccgcctttctcccttcgggaagcgtggcgctttctcaatg
2701  ---------+---------+---------+---------+---------+---------+ 2760

      ctcacgctgtaggtatctcagttcggtgtaggtcgttcgctccaagctgggctgtgtgca
2761  ---------+---------+---------+---------+---------+---------+ 2820

      cgaacccccccgttcagcccgaccgctgcgccttatccggtaactatcgtcttgagtccaa
2821  ---------+---------+---------+---------+---------+---------+ 2880

      cccggtaagacacgacttatcgccactggaagcagccactggtaacaggattagcagagc
2881  ---------+---------+---------+---------+---------+---------+ 2940

      gaggtatgtaggcggtgctacagagttcttgaagtggtggcctaactacggctacactag
2941  ---------+---------+---------+---------+---------+---------+ 3000

      aaggacagtatttggtatctgcgctctgctgaagccagttaccttcggaaaaagagttgg
3001  ---------+---------+---------+---------+---------+---------+ 3060

      tagctcttgatccggcaaacaaaccaccgctggtagcggtggtttttttgtttgcaagca
3061  ---------+---------+---------+---------+---------+---------+ 3120

      gcagattacgcgcagaaaaaaaggatctcaagaagatcctttgatcttttctacggggtc
3121  ---------+---------+---------+---------+---------+---------+ 3180

      tgacgctcagtggaacgaaaactcacgttaagggattttggtcatgagattatcaaaaag
3181  ---------+---------+---------+---------+---------+---------+ 3240

      gatcttcacctagatccttttaaattaaaaatgaagttttaaatcaatctaaagtatata
3241  ---------+---------+---------+---------+---------+---------+ 3300

      tgagtaaacttggtctgacagttaccaatgcttaatcagtgaggcacctatctcagcgat
3301  ---------+---------+---------+---------+---------+---------+ 3360

      ctgtctatttcgttcatccatagttgcctgactccccgtcgtgtagataactacgatacg
3361  ---------+---------+---------+---------+---------+---------+ 3420

      ggagggcttaccatctggccccagtgctgcaatgataccgcgagacccacgctcaccggc
3421  ---------+---------+---------+---------+---------+---------+ 3480

      tccagatttatcagcaataaaccagccagccggaagggccgagcgcagaagtggtcctgc
3481  ---------+---------+---------+---------+---------+---------+ 3540

      aactttatccgcctccatccagtctattaattgttgccgggaagctagagtaagtagttc
3541  ---------+---------+---------+---------+---------+---------+ 3600

      gccagttaatagtttgcgcaacgttgttgccattgctacaggcatcgtgtggtcacgctc
3601  ---------+---------+---------+---------+---------+---------+ 3660

      gtcgtttggtatggcttcattcagctccggttcccaacgatcaaggcgagttacatgatc
3661  ---------+---------+---------+---------+---------+---------+ 3720

      ccccatgttgtgcaaaaaagcggttagctccttcggtcctccgatcgttgtcagaagtaa
3721  ---------+---------+---------+---------+---------+---------+ 3780

      gttggccgcagtgttatcactcatggttatggcagcactgcataattctcttactgtcat
3781  ---------+---------+---------+---------+---------+---------+ 3840

      gccatccgtaagatgcttttctgtgactggtgagtactcaaccaagtcattctgagaata
3841  ---------+---------+---------+---------+---------+---------+ 3900

      gtgtatgcggcgaccgagttgctcttgcccgtcgtcaatacgggataataccgcgccaca
3901  ---------+---------+---------+---------+---------+---------+ 3960

      tagcagaactttaaaagtgctcatcattggaaaacgttcttcggggcgaaaactctcaag
```

Fig. 12

```
3961 ---------+---------+---------+---------+---------+---------+ 4020

     gatcttaccgctgttgagatccagttcgatgtaacccactcgtgcacccaactgatcttc
4021 ---------+---------+---------+---------+---------+---------+ 4080

     agcatcttttactttcaccagcgtttctgggtgagcaaaaacaggaaggcaaaatgccgc
4081 ---------+---------+---------+---------+---------+---------+ 4140

     aaaaaagggaataagggcgacacggaaatgttgaatactcatactcttccttttcaata
4141 ---------+---------+---------+---------+---------+---------+ 4200

     ttattgaagcatttatcagggttattgtctcatgagcggatacatatttgaatgtattta
4201 ---------+---------+---------+---------+---------+---------+ 4260

     gaaaaataaacaaatagggttccgcgcacatttccccgaaaagtgccacctgacgtcta
4261 ---------+---------+---------+---------+---------+---------+ 4320

     agaaaccattattatcatgacattaacctataaaaataggcgtatcacgaggccctttcg
4321 ---------+---------+---------+---------+---------+---------+ 4380

     tc
4381 -- 4382
```

Fig. 12